ile 155:MEDLINE(R) 1966-2000/Aug W2
(c) format only 2000 Dialog Corporation
*File 155: MEDLINE has been reloaded. Accession numbers have changed.

Web/DIALOG 6/30 VOF

Set	Items	Description
?ds		

Set	Items	Description
S1	380	E3-E17 Enterobacter
S2	380	R1-R3
S3	76	(S1 OR S2) AND (DNA OR CDNA OR CHROMOS?)
S4	38	S3/1996:2000
S5	38	S3 NOT S4

?t s5/9/11 15 22 24 28 29 30 32

5/9/11
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

08108005 95145174
Ribosomal DNA fingerprinting analysis of Enterobacter cloacae isolated from an outbreak of nosocomial infection]
Li P; Li GQ; Liu C
Shandong Provincial Hospital, Jinan.
Chung-hua yu fang i hsueh tsa chih (CHINA) Sep 1994, 28 (5) p278-80, ISSN 0253-9624 Journal Code: D74
Languages: CHINESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract
JOURNAL ANNOUNCEMENT: 9505
Subfile: INDEX MEDICUS
16s and 23s ribosomal **DNA** (rDNA) genes were amplified form E. coli, labelled with [alpha- 32P] dATP by nick translation, and applied as conserved gene probes to detecting broad-spectrum rDNA. rDNA fingerprinting analysis of Enterobacter cloacae (E. cloacae) isolated form an outbreak of nosocomial infection and other hospital environmental sources was conducted with digestion by different restrictive endonuclease, such as Hind III, EcoRI, BamHI, Bgl I, et al. Results showed rDNA fingerprinting of E. cloacae strains isolated from 10 patients with nosocomial infection was the same as that from other sources. It suggested E. cloacae causing this outbreak was originated from one genetic clone, and its source of infection was the tubes and humidifying bottles for oxygenation. rDNA fingerprinting technique is accurate, reliable, specific and repeatable, and will plays important roles in identification and classification of bacteria, tracking the source of transmission of nosocomial infection.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: Cross Infection--Microbiology--MI; ***DNA** Fingerprinting; ***DNA** , Bacterial--Genetics--GE; * **Enterobacter cloacae** --Genetics--GE; *Enterobacteriaceae Infections--Microbiology--MI; **DNA** , Ribosomal --Genetics--GE
CAS Registry No.: 0 (DNA, Bacterial); 0 (DNA, Ribosomal)

5/9/15
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

07976068 94329582
Analysis of a carbapenem-hydrolyzing class A beta-lactamase from Enterobacter cloacae and of its LysR-type regulatory protein.
Naas T; Nordmann P
Abteilung Mikrobiologie, Biozentrum der Universitat Basel, Switzerland.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 2 1994, 91 (16) p7693-7, ISSN 0027-8424 Journal Code: PV3
Languages: ENGLISH
Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9411
Subfile: INDEX MEDICUS

Carbapenems such as imipenem are extended-spectrum beta-lactam antibiotics, which are not hydrolyzed by the beta-lactamases commonly found in Enterobacteriaceae. Here we report a gene encoding a carbapenemase, which was cloned from the **chromosome** of a clinical isolate of Enterobacter cloacae, strain NOR-1, into pACYC184 plasmid in Escherichia coli. Unlike all the sequenced carbapenemases, which are class B metallo-beta-lactamases, the mature protein (NmcA) is a class A serine beta-lactamase. NmcA shares the highest amino acid identity (50%) with the extended-spectrum class A beta-lactamase MEN-1 from E. coli. In the opposite orientation from the nmcA promoter, an overlapping and divergent promoter was detected, along with an open reading frame, which encoded a 33.5-kDa protein (NmcR). The NmcR amino acid sequence displays homology with LysR-type transcriptional regulatory proteins, including the conserved residues near its N terminus within a helix-turn-helix motif. Deletion of nmcR resulted in decreased carbapenem resistance and a loss of beta-lactamase inducibility, demonstrating a positive role of NmcR in NmcA expression.

Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: beta-Lactamases--Genetics--GE; *Bacterial Proteins--Genetics--GE; *Carbapenems--Metabolism--ME; *Enterobacter cloacae --Genetics--GE; *Gene Expression Regulation; *Transcription Factors--Genetics--GE; Amino Acid Sequence; Base Sequence; Drug Resistance, Microbial--Genetics--GE; DNA Mutational Analysis; Enterobacter cloacae --Enzymology--EN; Gene Expression Regulation, Bacterial; Gene Expression Regulation, Enzymologic; Hydrolysis; Molecular Sequence Data; Restriction Mapping; Sequence Analysis ; Sequence Deletion; Sequence Homology, Amino Acid; Transcription, Genetic

Molecular Sequence Databank No.: GENBANK/Z21956

CAS Registry No.: 0 (Bacterial Proteins); 0 (Carbapenems); 0 (Transcription Factors); 87609-37-8 (LysR protein)

Enzyme No.: EC 3.5.2.- (NmcA protein); EC 3.5.2.6 (beta-Lactamases)

Gene Symbol: nmcA; lysR; nmcR

5/9/22

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2000 Dialog Corporation. All rts. reserv.

07769171 94119652

[Molecular markers and epidemiology of nosocomial infections in pediatric hospital units]

Marqueurs moleculaires et epidemiologie des infections nosocomiales en pediatrie.

Bingen E

Laboratoire de Microbiologie, Hopital Robert Debre, Paris, France.

Pathologie-biologie (FRANCE) Oct 1993, 41 (8) p716-23, ISSN 0369-8114 Journal Code: OSG

Languages: FRENCH Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE English Abstract

JOURNAL ANNOUNCEMENT: 9404

Subfile: INDEX MEDICUS

Nosocomial infection cause severe morbidity and mortality in pediatric patients. To find the cause of an infectious disease outbreak, epidemiologists need to determine early on whether a single strain of microorganism is responsible for the majority of cases. Phenotypic characteristics have been widely used in epidemiologic studies. However with most systems poor reproducibility, poor sensitivity have been reported and they do not reliably show enough strain-to-strain variation to be sufficiently discriminative. Molecular approaches like the analysis of the restriction fragment length polymorphism of the total **DNA** and of the rDNA regions and pulsed-field gel electrophoresis typing have now been applied with success to a large number of bacterial species associated with epidemics.

Tags: Human

Descriptors: Bacteria--Genetics--GE; *Cross Infection--Genetics--GE; * **DNA** , Bacterial--Genetics--GE; * **DNA** , Ribosomal--Genetics--GE;

Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9309
Subfile: INDEX MEDICUS

A clinical isolate of Enterobacter cloacae, strain NOR-1, exhibited resistance to imipenem and remained susceptible to extended-spectrum cephalosporins. Clavulanic acid partially restored the susceptibility of the strain to imipenem. Two beta-lactamases with isoelectric points (pI) of 6.9 and > 9.2 were detected in strain E. cloacae NOR-1; the higher pI corresponded to AmpC cephalosporinase. Plasmid **DNA** was not detected in E. cloacae NOR-1 and imipenem resistance could not be transferred into Escherichia coli JM109. The carbapenem-hydrolyzing beta-lactamase gene was cloned into plasmid pACYC184. One recombinant plasmid, pPTN1, harbored a 5.3-kb Sau3A fragment from E. cloacae NOR-1 expressing the carbapenem-hydrolyzing beta-lactamase. This enzyme (pI 6.9) hydrolyzed ampicillin, cephalothin, and imipenem more rapidly than it did meropenem and aztreonam, but it hydrolyzed extended-spectrum cephalosporins only weakly and did not hydrolyze cefoxitin. Hydrolytic activity was partially inhibited by clavulanic acid, sulbactam, and tazobactam, was nonsusceptible to chelating agents such as EDTA and 1,10-o-phenanthroline, and was independent of the presence of ZnCl2. Its relative molecular mass was 30,000 Da. Induction experiments concluded that the carbapenem-hydrolyzing beta-lactamase biosynthesis was inducible by cefoxitin and imipenem. Subcloning experiments with HindIII partial digests of pPTN1 resulted in a recombinant plasmid, designated pPTN2, which contained a 1.3-kb insert from pPTN1 and which conferred resistance to beta-lactam antibiotics. (ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Support, Non-U.S. Gov't

Descriptors: beta-Lactamases--Genetics--GE; *Carbapenems--Metabolism--ME; ***Enterobacter cloacae*** --Enzymology--EN; ***Enterobacter cloacae*** --Genetics --GE; *Escherichia coli--Enzymology--EN; *Escherichia coli--Genetics--GE; *Genes, Bacterial; beta-Lactamases--Biosynthesis--BI; Cloning, Molecular; Drug Resistance, Microbial; **DNA** , Bacterial--Chemistry--CH; Hydrolysis; Isoelectric Focusing; Microbial Sensitivity Tests; Molecular Weight; Nucleic Acid Hybridization; Sequence Homology, Nucleic Acid

CAS Registry No.: 0 (Carbapenems); 0 (DNA, Bacterial)

Enzyme No.: EC 3.5.2.6 (beta-Lactamases)

5/9/29

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2000 Dialog Corporation. All rts. reserv.

07507342 93186526

Effect of ampicillin versus cefuroxime on the emergence of beta-lactam resistance in faecal Enterobacter cloacae isolates from neonates.

Burman LG; Berglund B; Huovinen P; Tullus K

National Bacteriological Laboratory, Stockholm, Sweden.

Journal of antimicrobial chemotherapy (ENGLAND) Jan 1993, 31 (1) p111-6, ISSN 0305-7453 Journal Code: HD7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9306

Subfile: INDEX MEDICUS

Enterobacter cloacae strains dominated the aerobic faecal flora of 8.3- of 953 infants discharged from 32 Swedish neonatal intensive care units and the susceptibility of these strains to seven beta-lactam antibiotics was determined. Isolates from infants treated with cefuroxime showed slightly increased MICs only to ampicillin, cephalexin and cephalothin as compared to isolates from untreated infants matched for ward and time of sampling (P = 0.02). In contrast, E. cloacae isolates from ampicillin treated infants showed markedly elevated MICs of all agents tested including piperacillin, cefuroxime, cefotaxime and ceftazidime as compared to those from control neonates (P values between 0.001 for ampicillin and 0.017 for cefotaxime). Thus, E. cloacae with cefotaxime MICs as high as 512 mg/L were isolated only after ampicillin therapy. The resistant strains were negative in a colony **DNA** hybridization assay using gene probes for the plasmid

*Polymorphism, Restriction Fragment Length; Blotting, Southern; Child; Child, Preschool; **DNA** Fingerprinting; Electrophoresis, Gel, Pulsed-Field; **Enter bacter cloacae** --Genetics--GE; Hospital Units; Infant; Serratia marcescens--Genetics--GE
CAS Registry No.: 0 (DNA, Bacterial); 0 (DNA, Ribosomal)

5/9/24
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

07757135 93107247
Epidemiological fingerprinting of Enterobacter cloacae by small-fragment restriction endonuclease analysis and pulsed-field gel electrophoresis of genomic restriction fragments.
Haertl R; Bandlow G
Staatliches Medizinal-Untersuchungsamt Osnabruck, Germany.
Journal of clinical microbiology (UNITED STATES) Jan 1993, 31 (1) p128-33, ISSN 0095-1137 Journal Code: HSH
Languages: ENGLISH
Document type: JOURNAL ARTICLE
JOURNAL ANNOUNCEMENT: 9303
Subfile: INDEX MEDICUS
A cluster of infections caused by Enterobacter cloacae was observed among preterm neonates in a neonatal intensive care unit (NICU) of a pediatric hospital in Osnabruck, Germany. The presence of similar antimicrobial susceptibility patterns among the bacterial isolates prompted an investigation to determine whether a limited spread of a single strain existed. All 12 E. cloacae isolates from the NICU and 50 nonrelated strains were fingerprinted by small-fragment restriction endonuclease analysis (SF-REA) of EcoRI **DNA** digests. Selected isolates were further characterized by pulsed-field gel electrophoresis (PFGE) of NotI- or XbaI-generated genomic restriction fragments. Epidemiologically unrelated strains were clearly discriminated by both methods. Results achieved by SF-REA and PFGE revealed that of the 12 isolates from the NICU, 11 belonged to the same genotypic cluster. Since all reagents and equipment for both techniques are commercially available, **DNA** fingerprinting by SF-REA or PFGE is proposed as a useful tool in the microbiology laboratory for investigating the epidemiological relatedness of E. cloacae strains of clinical and environmental origin.
Tags: Human
Descriptors: **DNA** Fingerprinting--Methods--MT; ***Enterobacter cloacae** --Classification--CL; * **Enterobacter cloacae** --Genetics--GE; *Enterobacteriaceae Infections--Microbiology--MI; *Infant, Premature, Diseases--Microbiology--MI; Cross Infection--Microbiology--MI; Disease Outbreaks; **DNA** Restriction Enzymes; Electrophoresis, Gel, Pulsed-Field; Enterobacteriaceae Infections--Epidemiology--EP; Genotype; Germany --Epidemiology--EP; Infant, Newborn; Infant, Premature; Infant, Premature, Diseases--Epidemiology--EP; Intensive Care Units, Neonatal; Microbial Sensitivity Tests; Phenotype; Plasmids; Polymorphism, Restriction Fragment Length
CAS Registry No.: 0 (Plasmids)
Enzyme No.: EC 3.1.21 **DNA** Restriction Enzymes)

5/9/28
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2000 Dialog Corporation. All rts. reserv.

07567938 93297955
Biochemical properties of a carbapenem-hydrolyzing beta-lactamase from Enterobacter cloacae and cloning of the gene into Escherichia coli.
Nordmann P; Mariotte S; Naas T; Labia R; Nicolas MH
Laboratoire de Microbiologie, Hopital Raymond Poincare, Faculte de Medecine Paris-Ouest, Garches, France.
Antimicrobial agents and chemotherapy (UNITED STATES) May 1993, 37 (5) p939-46, ISSN 0066-4804 Journal Code: 6HK

beta-lactamases TEM-1, OXA-1 and SHV-1. The resistant strains also showed only one beta-lactamase band when crude cell sonicates were analysed by isoelectric focusing, and were not found in other infants in the same ward. The results indicate that the selection of **chromosomal** E. cloacae mutants, presumably with stably derepressed beta-lactamase production, in the faecal flora of neonates is rare during treatment with cefuroxime and more common during ampicillin therapy.

Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Descriptors: Ampicillin--Pharmacology--PD; *Antibiotics, Lactam --Pharmacology--PD; *Cefuroxime--Pharmacology--PD; ***Enterobacter cloacae** --Drug Effects--DE; Bacterial Typing Techniques; Drug Resistance, Microbial ; **Enterobacter cloacae** --Genetics--GE; **Enterobacter cloacae** --Isolation and Purification--IP; Feces--Microbiology--MI; Infant, Newborn; Microbial Sensitivity Tests; Sweden

CAS Registry No.: 0 (Antibiotics, Lactam); 55268-75-2 (Cefuroxime); 69-53-4 (Ampicillin)

5/9/30

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2000 Dialog Corporation. All rts. reserv.

07422410 92078085

Multiple copies of IS10 in the Enterobacter cloacae MD36 chromosome.

Matsutani S

National Institute of Hygienic Sciences, Tokyo, Japan.

Journal of bacteriology (UNITED STATES) Dec 1991, 173 (24) p7802-9, ISSN 0021-9193 Journal Code: HH3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9203

Subfile: INDEX MEDICUS

Repetitive sequences were isolated and characterized as double-stranded **DNA** fragments by treatment with S1 nuclease after denaturation and renaturation of the total **DNA** of Enterobacter cloacae **MD36**. One repetitive sequence was identical to the nucleotide sequence of IS10-right (IS10R), which is the active element in the plasmid-associated transposon Tn10. Unexpectedly, 15 copies of IS10R were found in the **chromosomal DNA** of E. cloacae MD36. One copy of the central region of Tn10 was found in the total **DNA** of E. cloacae MD36. IS10Rs in restriction fragments isolated from the E. cloacae MD36 total **DNA** showed 9-bp duplications adjacent to the terminal sequences that are characteristic of Tn10 transposition. This result suggests that many copies of IS10R in E. cloacae MD36 are due to transposition of IS10R alone, not due to transposition of Tn10 or to **DNA** rearrangement. I also found nine copies of IS10 in Shigella sonnei HH109, two and four copies in two different natural isolates of Escherichia coli, and two copies in E. coli K-12 strain JM109 from the 60 bacterial strains that were examined. All dam sites in the IS10s in E. cloacae MD36 and S. sonnei HH109 were methylated. Tn10 and IS10 transpose by a mechanism in which the element is excised from the donor site and inserted into the new target site without significant replication of the transposing segment; thus, the copy numbers of the elements in the cell are thought to be unchanged in most circumstances. Accumulation of IS10 copies in E. cloacae MD36 has interesting evolutionary implications.

Descriptors: **DNA** Transposable Elements; * **Enterobacter cloacae** --Genetics--GE; *Repetitive Sequences, Nucleic Acid; Base Sequence; Blotting, Southern; **Chromosomes** , Bacterial; Cloning, Molecular; **DNA** , Bacterial; Enterobacteriaceae--Genetics--GE; Methylation; Molecular Sequence Data; Mutation

Molecular Sequence Databank No.: GENBANK/D00950; GENBANK/D00951; GENBANK/D00952; GENBANK/S69596; GENBANK/S69601; GENBANK/S69604; GENBANK/S69828; GENBANK/S69830; GENBANK/M64332; GENBANK/M63255

CAS Registry No.: 0 (DNA Transposable Elements); 0 (DNA, Bacterial)

5/9/32

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2000 Dialog Corporation. All rts. reserv.

07266563 92314252

Molecular analysis provides evidence for the endogenous origin of bacteremia and meningitis due to Enterobacter cloacae in an infant.

Lambert-Zechovsky N; Bingen E; Denamur E; Brahimi N; Brun P; Mathieu H; Elion J

Laboratoire de Microbiologie, Hopital Robert Debre, Paris, France.

Clinical infectious diseases (UNITED STATES) Jul 1992, 15 (1) p36-2, ISSN 1058-4838 Journal Code: A4J

Languages: ENGLISH

Document type: JOURNAL ARTICLE

JOURNAL ANNOUNCEMENT: 9210

Subfile: INDEX MEDICUS

We analyzed the restriction fragment length polymorphism (RFLP) of total **DNA** and of ribosomal **DNA** regions (ribotyping) to document the occurrence of endogenous, systemic bacteremia and meningitis due to Enterobacter cloacae in a newborn. Five strains of E. cloacae were isolated from this newborn. Three of these strains were recovered from stool at counts of 10(8), 10(9), and 10(9) organisms/g of feces, respectively; one strain was isolated from blood; and one strain was isolated from cerebrospinal fluid. In addition, five epidemiologically unrelated strains of E. cloacae were studied for comparison. Our study clearly shows the genetic relatedness of the strains isolated sequentially from cultures of stool, blood, and cerebrospinal fluid. RFLP analysis of total **DNA** and ribotyping seem particularly well suited to the study of the epidemiology of nosocomial E. cloacae strains.

Tags: Case Report; Human; Male

Descriptors: Bacteremia--Microbiology--MI; * **DNA** , Bacterial--Analysis --AN; ***Enterobacter cloacae*** --Genetics--GE; *Enterobacteriaceae Infections --Etiology--ET; *Meningitis, Bacterial--Microbiology--MI; **DNA** , Ribosomal --Analysis--AN; ***Enterobacter cloacae*** --Isolation and Purification--IP; Enterobacteriaceae Infections--Diagnosis--DI; Infant, Newborn; Polymorphism, Restriction Fragment Length

CAS Registry No.: 0 (DNA, Bacterial); 0 (DNA, Ribosomal)

?logoff hold

19jun00 13:57:05 User228206 Session D1235.3

$1.21 0.378 DialUnits File155

$1.60 8 Type(s) in Format 9

$1.60 8 Types

$2.81 Estimated cost File155

$0.05 TYMNET

$2.86 Estimated cost this search

$2.86 Estimated total session cost 0.378 DialUnits

Status: Signed Off. (1 minutes)

updated 1/01 VOP

```
      (c) 2001 AMERICAN CHEMICAL SOCIETY
*File 399: Use is subject to the terms of your user/customer agreement.
RANK charge added; see HELP RATES 399.
  File 434:SciSearch(R) Cited Ref Sci  1974-1989/Dec
        (c) 1998 Inst for Sci Info
*File 434: Please note new price changes effective January 1, 2001.
See Help Rates434 for details.
  File 442:AMA  Journals  1982-2000/Oct B3
        (c)2000 Amer Med Assn -FARS/DARS apply
*File 442: There is no data missing. UDs have been adjusted to reflect
the current months data. See Help News442 for details.
  File 444:New England Journal of Med.  1985-2001/Jan W4
        (c) 2001 Mass. Med. Soc.
*File 444: UDs have been adjusted to reflect the current months data.
There is no data missing.
  File 457:The Lancet  1986-2000/Oct W1
        (c) 2000 The Lancet, Ltd.
*File 457: Due to production changes at The Lancet, the updating of
this file is delayed.
  File 467:ExtraMED(tm)  2000/Dec
        (c) 2001 Informania Ltd.

      Set  Items  Description
      ---  -----  -----------
?ds

Set     Items   Description
S1       6284   E3-E50
S2         18   E1-E9
S3         14   "ENTEROBACTER CLOACAE, INTRATHECAL AND INTRACIS" OR "ENTER-
                  OBACTER CLOACEA (ENTEROBACTERIACEAE)" OR "ENTEROBACTER CLOACE-
                  AE" OR "ENTEROBACTER CLOACEAE (ENTEROBACTERIACEAE)" OR "ENTER-
                  OBACTER CLOAEAE" OR "ENTEROBACTER CLOCAE"
S4          1   "ENTEROBACTER CHOACAE"
S5       6344   "ENTEROBACTER CLOACAE" OR DC="B3.40.40.40.25" OR DC="B3.44-
                  0.450.425.275.200." OR DC="B3.660.250.150.170.100."
S6       1621   R1-R2
S7       1621   R1-R2
S8       1621   R1-R2
S9          1   (S1-S8) (5N) (VACCIN? OR VACIN?)
S10        11   (S1-S8) (10N) (VACCIN? OR INJECT?)
S11         7   (S1-S8) (10N) (IMMUNIZ? OR IMMUNIS?)
S12        18   S10 OR S11
S13        16   RD (unique items)
?t s13/9/11 7 3
```

Identification of factors affecting in vivo aminoglycoside activity in an experimental model of gram-negative endocarditis

Potel G.; Caillon J.; Le Gallou F.; Bugnon D.; Le Conte P.; Raza J.; Lepage - J.Y.; Baron D.; Drugeon H.

Lab. d'Antibiologie Clin. et Exptl., Faculte de Medecine, 1 rue Gaston-Veil,44035 Nantes France

Antimicrobial Agents and Chemotherapy (ANTIMICROB. AGENTS CHEMOTHER.) (United States) 1992, 36/4 (744-750)

CODEN: AMACC ISSN: 0066-4804

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Aminoglycoside bactericidal activity during the first 24 hr of treatment probably is a determining parameter in the prognosis of severe gram-negative infections in immunocompromised patients. To identify the predictive factors involved in the definition of the best therapeutic regimen for Enterobacter cloacae and Serratia marcescens infections, we studied different gentamicin, tobramycin, and amikacin regimens by using an experimental model of rabbit endocarditis. Two factors appear to play an important role in predicting in vivo efficacy: (i) the level of in vivo bactericidal activity, which can differ widely from one aminoglycoside to another for the same bacterial strain and from one strain to another of the same species, and (ii) the critical serum drug concentration (CSC, in milligrams per liter), defined as the lowest serum antibiotic concentration capable of producing a significant CFU reduction ($P < 0.05$) in endocarditis vegetations 24 h after the beginning of a continuous infusion. Stepwise regression analysis showed that for gentamicin and S. marcescens, the area under the concentration-time curve above the CSC and then the time above the CSC are the determining parameters for efficacy ($R = 0.69$; $F = 13.5$; $P = 0.001$), whereas for amikacin and S. marcescens, the time above the CSC and then the area under the concentration- time curve above the CSC predict efficacy ($R = 0.74$; $F = 24.0$; $P = 0.0001$). The lowest CSC is that of amikacin (about 8 mg/liter); those of gentamicin and tobramycin are about 15 mg/liter. In severe S. marcescens infections, intermittent amikacin dosing offers excellent bactericidal activity within the first 24 h.

MANUFACTURER NAMES: lilly; schering plough; bristol

DRUG DESCRIPTORS:

```
File 155:MEDLINE(R)  1966-2004/Jan W2
       (c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.

      Set  Items  Description
      ---  -----  -----------
?e enterobacter cloacae

Ref    Items    RT  Index-term
E1         2        ENTEROBACTER AEROGENES --PATHOGENICITY --PY
E2         5        ENTEROBACTER AEROGENES --PHYSIOLOGY --PH
E3       544     3 *ENTEROBACTER CLOACAE
E4        11        ENTEROBACTER CLOACAE --CHEMISTRY --CH
E5        40        ENTEROBACTER CLOACAE --CLASSIFICATION --CL
E6         5        ENTEROBACTER CLOACAE --CYTOLOGY --CY
E7       175        ENTEROBACTER CLOACAE --DRUG EFFECTS --DE
E8       146        ENTEROBACTER CLOACAE --ENZYMOLOGY --EN
E9       140        ENTEROBACTER CLOACAE --GENETICS --GE
E10       47        ENTEROBACTER CLOACAE --GROWTH AND DEVELOPMENT
E11       11        ENTEROBACTER CLOACAE --IMMUNOLOGY --IM
E12      120        ENTEROBACTER CLOACAE --ISOLATION AND PURIFICAT

          Enter P or PAGE for more
?p

Ref    Items    RT  Index-term
E13       49        ENTEROBACTER CLOACAE --METABOLISM --ME
E14       11        ENTEROBACTER CLOACAE --PATHOGENICITY --PY
E15       20        ENTEROBACTER CLOACAE --PHYSIOLOGY --PH
E16        7        ENTEROBACTER CLOACAE --RADIATION EFFECTS --RE
E17       12        ENTEROBACTER CLOACAE --ULTRASTRUCTURE --UL
E18        1        ENTEROBACTER CLOACAE --VIROLOGY --VI
E19        1     3  ENTEROBACTER SAKAZAKII
E20        1        ENTEROBACTER SAKAZAKII --ISOLATION AND PURIFIC
E21        1        ENTEROBACTER SAKAZAKII --PATHOGENICITY --PY
E22        2        ENTEROBACTERACEAE
E23        1        ENTEROBACTERACEAL
E24        1        ENTEROBACTERACIAE

          Enter P or PAGE for more
?s e10 or e12
              47  ENTEROBACTER CLOACAE --GROWTH AND DEVELOPMENT
             120  ENTEROBACTER CLOACAE --ISOLATION AND PURIFICAT
      S1     156  'ENTEROBACTER CLOACAE --GROWTH AND DEVELOPMENT' OR
                  'ENTEROBACTER CLOACAE --ISOLATION AND PURIFICAT'
?s s1/1998:2003
             156  S1
         2968759  PY=1998 : PY=2003
      S2      81  S1/1998:2003
?s s1 not s2
             156  S1
              81  S2
      S3      75  S1 NOT S2
? s s3 and (grow? or cultur?)
              75  S3
          789303  GROW?
          796823  CULTUR?
      S4      33  S3 AND (GROW? OR CULTUR?)
?s s4 and (varian? or recombin? or plasmid? or differ?)
              33  S4
          219339  VARIAN?
          257812  RECOMBIN?
           94806  PLASMID?
         2224874  DIFFER?
      S5       9  S4 AND (VARIAN? OR RECOMBIN? OR PLASMID? OR DIFFER?)
?t s4/9/all

 4/9/1
```

1/04 BP updated

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10907798 97259825 PMID: 9105924
Quality control of two rose bengal and modified DRBC and DG18 media.
Olsen M; Andersson K; Akerstrand K
Biology Division, National Food Administration, Uppsala, Sweden. mool@slv.se
International journal of food microbiology (NETHERLANDS) Apr 1 1997, 35 (2) p163-8, ISSN 0168-1605 Journal Code: 8412849
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The effect of storage on the performance of four mycological media, DG18, DRBC and two Rose Bengal agars, one from Difco, the other recommended by the Swedish Standard Institution, was investigated. The autoclaved media were stored (+4 degrees C) in the dark for up to 26 weeks. Following each storage period, the media were remelted and poured and the plates stored (+4 degrees C) in the dark for a maximum of 8 weeks before inoculation with test microorganisms. All media contained antibiotics. Both rapidly and slowly **growing** moulds, and also yeasts and bacteria were used as test microorganisms. No distinct effect of storage time on colony appearance could be shown for any of the four media. If the loss of restricted **growth** of Rhizopus stolonifer is used as a measure of the performance of the media, DRBC plates should not be stored for longer than 2 weeks after being poured from fresh medium. Storage of DRBC in flasks should not exceed 4 weeks and plates prepared from this medium should not be kept for more than 1 week. DG18 plates should only be poured from fresh medium and kept for a maximum of 1 week. The inhibitory effect of the antibiotic supplement on bacteria lasted for at least 4 weeks in DG18 and the two rose bengal media.
Tags: Comparative Study
Descriptors: **Culture** Media--standards--ST; *Rose Bengal--standards--ST ; Agar; Antibiotics--pharmacology--PD; Bacillus subtilis--drug effects--DE; Bacillus subtilis-- **growth** and development--GD; Cladosporium-- **growth** and development--GD; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli --drug effects--DE; Escherichia coli-- **growth** and development--GD; Food Microbiology; Heat; Microbiological Techniques; Penicillium-- **growth** and development--GD; Pseudomonas--drug effects--DE; Pseudomonas-- **growth** and development--GD; Quality Control; Rhizopus-- **growth** and development--GD; Sweden; Time Factors
CAS Registry No.: 0 (Antibiotics); 0 (Culture Media); 11121-48-5 (Rose Bengal); 9002-18-0 (Agar)
Record Date Created: 19970613
Record Date Completed: 19970613

4/9/2
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10727770 97077215 PMID: 8919782
Degradation of pentaerythritol tetranitrate by Enterobacter cloacae PB2.
Binks P R; French C E; Nicklin S; Bruce N C
Institute of Biotechnology, University of Cambridge, United Kingdom.
Applied and environmental microbiology (UNITED STATES) Apr 1996, 62 (4) p1214-9, ISSN 0099-2240 Journal Code: 7605801
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
A mixed microbial **culture** capable of metabolizing the explosive pentaerythritol tetranitrate (PETN) was obtained from soil enrichments under aerobic and nitrogen-limiting conditions. A strain of Enterobacter cloacae, designated PB2, was isolated from this **culture** and was found to use PETN as a sole source of nitrogen for **growth** . **Growth** yields

suggested that 2 to 3 mol of nitrogen was utilized per mol of PETN. The metabolites pentaerythritol dinitrate, 3-hydroxy-2,2-bis-[(nitrooxy)methyl] propanal, and 2,2-bis-[(nitrooxy)methyl]-propanedial were identified by mass spectrometry and 1H-nuclear magnetic resonance. An NADPH-dependent PETN reductase was isolated from cell extracts and shown to liberate nitrite from PETN, producing pentaerythritol tri- and dinitrates which were identified by mass spectrometry. PETN reductase was purified to apparent homogeneity by ion-exchange and affinity chromatography. The purified enzyme was found to be a monomeric flavoprotein with a M(r) of approximately 40,000, binding flavin mononucleotide noncovalently.

Tags: Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Enterobacter cloacae--metabolism--ME; *Pentaerythritol Tetranitrate--metabolism--ME; Aerobiosis; Biodegradation; **Enterobacter cloacae** --isolation and purification--IP; Environmental Pollutants --metabolism--ME; Kinetics; Oxidoreductases--isolation and purification--IP ; Oxidoreductases--metabolism--ME; Soil Microbiology; Substrate Specificity

Molecular Sequence Databank No.: GENBANK/U68759

CAS Registry No.: 0 (Environmental Pollutants); 78-11-5 (Pentaerythritol Tetranitrate)

Enzyme No.: EC 1. (Oxidoreductases); EC 1.7.99.- (pentaerythritol tetranitrate reductase)

Record Date Created: 19970102

Record Date Completed: 19970102

4/9/3

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

10595549 96413081 PMID: 8816296

Abscedation of posterior fossa dermoid cysts.

Tekkok I H; Baeesa S S; Higgins M J; Ventureyra E C

Division of Neurosurgery, Children's Hospital of Eastern Ontario, Ottawa, Canada.

Child's nervous system - ChNS - official journal of the International Society for Pediatric Neurosurgery (GERMANY) Jun 1996, 12 (6) p318-22, ISSN 0256-7040 Journal Code: 8503227

Comment in Childs Nerv Syst. 1997 Jun;13(6) 297; Comment in PMID 9272284

Document type: Journal Article; Review; Review of Reported Cases

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Dermoid cysts of the posterior fossa are uncommon. When associated with a dermal sinus, these cysts are often diagnosed during early childhood. The main risk of such an association is contamination of the cyst leading to abscedation of the dermoid itself or formation of daughter abscesses within the cerebellar hemisphere. We recently treated a 20-month-old girl who had a congenital dermal sinus leading to an intradural dermoid cyst. In addition to the midline dermoid cyst, computerized tomography revealed an enhancing lesion extending into the adjacent left cerebellar hemisphere. Suboccipital craniectomy was undertaken after 2 days of external ventricular drainage, and the infected dermoid and adjacent cerebellar abscess were excised. **Cultures** of the operative specimen revealed Corynobacterium aquaticum, Enterobacter sakazakii and Enterobacter cloacae, requiring 6 weeks of intravenous antibiotic therapy consisting of ceftriaxone, penicillin and gentamicin. A diligent literature search revealed only 24 sporadic cases reported over a period of 56 years. All 24 cases were in children (mean age 17 months), and one-third were in infants under the age of 1 year. All but 1 of these patients underwent posterior fossa surgery, with mortality and morbidity rates of 13% and 10%, respectively. Eleven (40%) children had suppuration within the cerebellar parenchyma, while the rest had abscedation of the dermoid cyst alone. Among the cases reviewed S. aureus was the most common agent, occurring with a probability of 64%. Key issues for appropriate management of these benign lesions are discussed. (24 Refs.)

Tags: Case Report; Female; Human

Descriptors: *Cranial Fossa, Posterior--surgery--SU; *Dermoid Cyst

Subfile: INDEX MEDICUS

The initial adhesion of microbes to tissue and solid surfaces can be mediated by hydrophobic interaction. Expression of microbial cell surface hydrophobicity (CSH) is influenced by **growth** conditions, and often best expressed after **growth** under nutrient-poor conditions, or "starvation". In the present study, the CSH of 133 strains of Enterobacteriaceae, Staphylococcus aureus, coagulase-negative staphylococci, Enterococcus faecalis, group A streptococcus, Pseudomonas aeruginosa, Clostridium perfringens, Bacteroides fragilis, Peptococcus magnus, and of 8 Candida albicans strains was measured by the salt aggregation test after **growth** on hematin agar in a 5% CO2 atmosphere, or under anaerobiosis. Cells of all but 8 strains expressed pronounced or moderate CSH, i.e., they aggregated in 0.01-2 M ammonium sulfate. When the agar surface was covered by human serum (diluted 1:5) to mimic **growth** conditions in a wound, 94 strains expressed higher CSH, and 44 strains the same CSH as after **growth** without serum. The CSH of 12 strains of different species was measured after **growth** on blood, hematin and PDM agar, with or without serum, and in an aerobic or a 5% CO2 atmosphere. The highest CSH was expressed after **growth** in 5% CO2 with serum, and the lowest **growth** after on blood agar in aerobic atmosphere. Identical results were obtained with native and heat-inactivated (56 C, 20 min) serum. The reduced surface tension obtained in 5% CO2, as well as yet unidentified serum factors, promotes expression of CSH.

Tags: Support, Non-U.S. Gov't

Descriptors: Bacterial Adhesion; *Staphylococcal Infections--microbiology --MI; *Staphylococcus-- **growth** and development--GD; *Wounds and Injuries --microbiology--MI; Cell Membrane--chemistry--CH; Cell Membrane --microbiology--MI; **Enterobacter cloacae** -- **growth** and development--GD; Enterobacter cloacae--pathogenicity--PY; Escherichia coli-- **growth** and development--GD; Escherichia coli--pathogenicity--PY; Pseudomonas aeruginosa-- **growth** and development--GD; Pseudomonas aeruginosa --pathogenicity--PY; Staphylococcus--pathogenicity--PY; Staphylococcus --physiology--PH; Surface Properties

Record Date Created: 19960314

Record Date Completed: 19960314

4/9/6

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

10319571 96121807 PMID: 7500636

Antibacterial activity of Helichrysum aureonitens (Asteraceae).

Meyer J J; Afolayan A J

Botany Department, University of Pretoria, South Africa.

Journal of ethnopharmacology (IRELAND) Jul 7 1995, 47 (2) p109-11, ISSN 0378-8741 Journal Code: 7903310

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The antibacterial activity of extracts from Helichrysum aureonitens was investigated. The dichloromethane extract was active against all five gram positive bacteria tested and the methanol extract was active only against Bacillus cereus, B. pumilus and Micrococcus kristinae, while the water extract had no activity against any of the organisms. None of the extracts inhibited the **growth** of the five gram negative bacteria tested.

Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: *Anti-Infective Agents--pharmacology--PD; *Gram-Positive Bacteria--drug effects--DE; *Plant Extracts--pharmacology--PD; Bacillus --drug effects--DE; Bacillus-- **growth** and development--GD; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli--drug effects--DE; Escherichia coli-- **growth** and development--GD; Gram-Positive Bacteria-- **growth** and development--GD; Klebsiella pneumoniae--drug effects--DE; Klebsiella pneumoniae-- **growth** and development--GD; Microbial Sensitivity Tests; Micrococcus--drug effects--DE; Micrococcus-- **growth** and development--GD; Pseudomonas aeruginosa--drug effects--DE; Pseudomonas aeruginosa-- **growth**

--surgery--SU; Corynebacterium--isolation and purification--IP; Cranial Fossa, Posterior--microbiology--MI; Cranial Fossa, Posterior--radiography --RA; Dermoid Cyst--microbiology--MI; Dermoid Cyst--radiography--RA; Enterobacter--isolation and purification--IP; **Enterobacter cloacae** --isolation and purification--IP; Infant; Radiographic Image Enhancement; Skull Base Neoplasms--microbiology--MI; Skull Base Neoplasms--radiography --RA; Skull Base Neoplasms--surgery--SU; Tomography, X-Ray Computed; Treatment Outcome
Record Date Created: 19961119
Record Date Completed: 19961119

4/9/4
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10539883 96351301 PMID: 8742359
Isolation and modulation of growth **of a colonization-impaired strain of Enterobacter cloacae in cucumber spermosphere.**
Roberts D P; Marty A M; Dery P D; Hartung J S
Biocontrol of Plant Diseases Laboratory, U.S. Department of Agriculture, Beltsville, MD 20705, U.S.A.
Canadian journal of microbiology (CANADA) Feb 1996, 42 (2) p196-201, ISSN 0008-4166 Journal Code: 0372707
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Enterobacter cloacae A-46 was isolated for use in an environmental containment strategy for genetically modified derivative strains with enhanced biocontrol activity. The population of E. cloacae A-46, a transposon mutant of the plant-beneficial bacterium E. cloacae 501R3, increased 10-fold (significant increase at P < or = 0.05) in cucumber spermosphere when applied to cucumber seeds along with casamino acids. In contrast, strain A-46 was incapable of proliferation in cucumber spermosphere in the absence of casamino acids. Populations of strain A-46 also failed to increase in corn, cowpea, sunflower, and wheat spermospheres in the absence of casamino acids, while populations of strain 501R3 increased 3162-, 512-, 1698-, and 93-fold, respectively. In addition, the persistence of strain A-46 in corn, cucumber, and sunflower rhizospheres and in natural soil was greatly reduced compared with the parental strain 501R3.
Tags: Comparative Study
Descriptors: Cucumis sativus--microbiology--MI; * **Enterobacter cloacae** --**growth** and development--GD; **Culture** Media; Enterobacter cloacae --genetics--GE; **Enterobacter cloacae** --isolation and purification--IP; Mutagenesis, Insertional; Plants--microbiology--MI; Seeds; Species Specificity; Time Factors
CAS Registry No.: 0 (Culture Media)
Record Date Created: 19961011
Record Date Completed: 19961011

4/9/5
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10353665 96156436 PMID: 8577265
Growth **conditions influence expression of cell surface hydrophobicity of staphylococci and other wound infection pathogens.**
Ljungh A; Wadstrom T
Department of Medical Microbiology, University of Lund, Sweden.
Microbiology and immunology (JAPAN) 1995, 39 (10) p753-7, ISSN 0385-5600 Journal Code: 7703966
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

and development--GD; Serratia marcescens--drug effects--DE; Serratia marcescens-- **growth** and development--GD; Staphylococcus aureus --drug effects--DE; Staphylococcus aureus-- **growth** and development--GD
CAS Registry No.: 0 (Anti-Infective Agents); 0 (Plant Extracts)
Record Date Created: 19960118
Record Date Completed: 19960118

4/9/7
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10288286 96090151 PMID: 7487027
Characterization of rhizosphere colonization by luminescent Enterobacter cloacae at the population and single-cell levels.
Rattray E A; Prosser J I; Glover L A; Killham K
Department of Plant and Soil Science, University of Aberdeen, United Kingdom.
Applied and environmental microbiology (UNITED STATES) Aug 1995, 61 (8) p2950-7, ISSN 0099-2240 Journal Code: 7605801
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
A bioluminescence marker system was used to characterized colonization of the rhizosphere by a bacterial inoculum, both in terms of population activity and at the single-cell level. Plasmid pQF70/44, which contains luxAB genes under the control of a strong constitutive phage promoter, was introduced into the rhizobacterium and model biocontrol agent Enterobacter cloacae. Light output from the lux-modified strain was detected by luminometry of samples from **growing cultures** of E. cloacae and from inoculated soil and wheat root samples. The minimum detection limits for fully active cells under optimum conditions were 90 and 445 cells g-1 for liquid **culture** and soil, respectively. The metabolic activities of the lux-marked population of E. cloacae, characterized by luminometry, contrasted in rhizosphere and nonrhizosphere soil. Cells in the rhizosphere were active, and there was a linear relationship between light output and cell concentration. The activity of cells in nonrhizosphere coil could not be detected unless the soil was supplied with substrate. Novel use of a charge-coupled device is reported for the spatial characterization of rhizosphere colonization by E. cloacae (pQF70/44) at the single-cell and population levels. Used macroscopically, the charge-coupled device identified differences in colonization due to competition from indigenous soil organisms. The lux-marked bacterium was able to colonize all depths of roots in the absence of competition but was restricted tot he spermosphere in the presence of competition (nonsterile soil).(ABSTRACT TRUNCATED AT 250 WORDS)
Tags: Support, Non-U.S. Gov't
Descriptors: **Enterobacter cloacae** -- **growth** and development--GD; Biological Markers; Biomass; Enterobacter cloacae--genetics--GE; **Enterobacter cloacae** --isolation and purification--IP; Genes, Bacterial; Luminescence; Soil Microbiology; Triticum--microbiology--MI
CAS Registry No.: 0 (Biological Markers)
Gene Symbol: luxAB
Record Date Created: 19951215
Record Date Completed: 19951215

4/9/8
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10263675 96065385 PMID: 7592171
Control-related effective regrowth time and post-antibiotic effect of meropenem on gram-negative bacteria studied by bioluminescence and viable counts.
Hanberger H; Svensson E; Nilsson L E; Nilsson M
Department of Infectious Diseases, University Hospital, Linkoping,

Sweden.
Journal of antimicrobial chemotherapy (ENGLAND) May 1995, 35 (5) p585-92, ISSN 0305-7453 Journal Code: 7513617
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

A study was performed to compare viable counts and bioluminescence for determining control related effective regrowth time (CERT) and postantibiotic effect (PAE) on Gram-negative bacteria after two hours of exposure to meropenem. There was a good correlation between bioluminescence and viable counts in determining the cell numbers in **growing cultures** of Escherichia coli. CERT was defined as the time required for the resumption of logarithmic **growth** and an increase of 1 log10 to occur over the pre-exposure inoculum in the test **culture** minus corresponding time for the control **culture** . PAE and CERT were studied on reference strains of Enterobacter cloacae, E. coli, Klebsiella pneumoniae and Pseudomonas aeruginosa. At 4 x MIC of meropenem the CERTs of these four Gram-negative strains were 4.1, 4.9, 4.2, and 3.6 h, respectively, when assayed by bioluminescence. Corresponding CERTs using viable counts were 4.2, 5.0, 5.1 and 3.8 h, respectively. In contrast to this good agreement between the methods in assessing CERT, the corresponding PAEs were highly method dependent. At 4 x MIC of meropenem the PAEs on E. cloacae, E. coli, K. pneumoniae and P. aeruginosa were 3.9, 4.8, 4.7, and 3.5 h, respectively, when assayed by bioluminescene. However, the corresponding and simultaneously determined viable count PAEs were -0.4, 0.5, -0.1, and 0.7 h, respectively. The poor correlation between these methods in assessing the PAE is caused by greater initial decrease in viability compared with the less prominent initial change in cell density as measured by bioluminescence.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: *Gram-Negative Bacteria--drug effects--DE; *Thienamycins --pharmacology--PD; Colony Count, Microbial--methods--MT; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli--drug effects--DE; Escherichia coli-- **growth** and development--GD; Gram-Negative Bacteria-- **growth** and development--GD; Klebsiella pneumoniae--drug effects--DE; Klebsiella pneumoniae-- **growth** and development--GD; Luminescence, Bacterial; Pseudomonas aeruginosa--drug effects--DE; Pseudomonas aeruginosa-- **growth** and development--GD

CAS Registry No.: 0 (Thienamycins); 96036-03-2 (meropenem)
Record Date Created: 19951130
Record Date Completed: 19951130

4/9/9
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08715403 95404008 PMID: 7673746

An outbreak of Enterobacter cloacae associated with contamination of a blood gas machine.

Lacey S L; Want S V
Department of Infectious Diseases and Bacteriology, Hammersmith Hospital, London, U.K.

Journal of infection (ENGLAND) May 1995, 30 (3) p223-6, ISSN 0163-4453 Journal Code: 7908424
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Over a 3-month period, five cases of Enterobacter cloacae bacteraemia occurred on our neonatal unit. In at least three of these, isolation of the organism coincided with clinical deterioration and evidence of sepsis. In one case, the same strain was isolated from an abscess on the neonate's forearm. The isolates had identical sensitivity patterns being resistant to all beta-lactams tested except imipenem. The extended time course of the

infections made cross-infection an unlikely explanation. Moreover, close questioning of the staff and observation of their practices with regard to blood **culture** collection, failed to reveal any likely mechanism for pseudobacteraemia. On extensive investigation of the environment to try to identify a potential source of the organism, a strain of Enterobacter cloacae, was isolated from the probe of the blood gas machine and the probe cover. No other environmental samples were found to harbour the organism. Subsequent typing procedures showed the blood gas isolate to be indistinguishable from the clinical isolates. Five neonates were successfully treated with imipenem and gentamicin. The exact mechanism whereby these bacteraemias occurred remains obscure. In one case, the baby had positive blood **cultures** within 2 h of being on the unit and contamination of the blood **culture** bottle by the doctor taking the **culture** was suspected. Most of the episodes, however, appeared clinically to be genuine septicaemias. When vigorous infection control procedures were instituted to prevent staff acquisition of the organism from the machine, cases on the unit ceased.

Tags: Human

Descriptors: *Bacteremia--etiology--ET; *Blood Gas Analysis --instrumentation--IS; *Cross Infection--etiology--ET; *Disease Outbreaks; *Enterobacter cloacae; *Enterobacteriaceae Infections--etiology--ET; *Equipment Contamination; Antibiotics, Aminoglycoside--therapeutic use--TU; Bacteremia--microbiology--MI; Bacterial Typing Techniques; Cross Infection --epidemiology--EP; Cross Infection--microbiology--MI; Enterobacter cloacae--classification--CL; **Enterobacter cloacae** --isolation and purification--IP; Enterobacteriaceae Infections--epidemiology--EP; Enterobacteriaceae Infections--microbiology--MI; Gentamicins--therapeutic use--TU; Imipenem--therapeutic use--TU; Infant; Infant, Newborn; Infection Control--methods--MT; Thienamycins--therapeutic use--TU

CAS Registry No.: 0 (Antibiotics, Aminoglycoside); 0 (Gentamicins); 0 (Thienamycins); 74431-23-5 (Imipenem)

Record Date Created: 19951017

Record Date Completed: 19951017

4/9/10

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

08578068 95266370 PMID: 7747531

The microbial flora in venous leg ulcers without clinical signs of infection. Repeated culture **using a validated standardised microbiological technique.**

Hansson C; Hoborn J; Moller A; Swanbeck G

Department of Dermatology, Sahlgrens' Hospital, Goteborg University, Sweden.

Acta dermato-venereologica (NORWAY) Jan 1995, 75 (1) p24-30, ISSN 0001-5555 Journal Code: 0370310

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The change of ulcer size in relation to the presence of species and quantities of microorganisms was analysed in 58 patients with venous leg ulcers, all without clinical signs of infection. Microbiological samples were taken on the day of inclusion and then repeated 4 times at monthly intervals or until the ulcer had healed or was too small to be **cultured** from. There was **growth** of microorganisms in all ulcers, and the numbers were below 10(4) per mm2 of ulcer surface in all cases. No correlation was found between ulcer size change and the species and amounts of microorganisms. Sixty-nine species were isolated. Staphylococcus aureus was found in 88%, Enterococcus faecalis in 74%, Enterobacter cloacae and Peptococcus magnus in 29%, and fungi in 11% of the samples. One or more obligate anaerobe species was found in 41% of the samples and in half of the ulcers and constituted 62% of all bacterial species. The colonising ulcer flora was markedly constant over time in the individual ulcers regardless of change in size. Resident bacterial species were found in 57 of the 58 ulcers. If all samples were considered, the microorganisms were

associated with not more than one fifth of the variability in healing rate, as shown by linear multiple regression analysis. The same species of microorganisms were found in ulcers that decreased (or healed) and in those that increased in size. Although an association between the microorganisms and ulcer healing could not be ruled out in this study, there seems to be no indication for routinely performed **culture** in the absence of clinical signs of infection in venous leg ulcers.

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: *Varicose Ulcer--microbiology--MI; Aged; Bacteriological Techniques; Bandages; Candida albicans--isolation and purification--IP; Colony Count, Microbial; **Enterobacter cloacae** --isolation and purification --IP; Enterococcus faecalis--isolation and purification--IP; Follow-Up Studies; Linear Models; Peptococcus--isolation and purification--IP; Pseudomonas aeruginosa--isolation and purification--IP; Skin--microbiology --MI; Staphylococcus aureus--isolation and purification--IP; Varicose Ulcer --pathology--PA; Varicose Ulcer--therapy--TH; Wound Healing

Record Date Created: 19950609

Record Date Completed: 19950609

4/9/11

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

08406070 95094085 PMID: 8000961

The optimization and application of two direct viable count methods for bacteria in distributed drinking water.

Coallier J; Prevost M; Rompre A; Duchesne D

Ecole Polytechnique de Montreal, Department of Civil Engineering, Environment, QC, Canada.

Canadian journal of microbiology (CANADA) Oct 1994, 40 (10) p830-6, ISSN 0008-4166 Journal Code: 0372707

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The optimal incubation conditions for the direct viable count method with nalidixic acid were determined. They do not differ from those proposed in the literature for a laboratory strain and a mixed bacterial population isolated from drinking water. The direct viable count method with 5-cyano-2,3-ditolyl tetrazolium chloride (CTC) was performed under in situ conditions. The bacteria were incubated with CTC at concentration of 1 mM for 4-6 h at the temperature of the water in the pipes and without the addition of an exogenous substrate. The results obtained for a laboratory strain using the two direct count methods were similar. However, for a mixed bacterial population, the counts were always higher with the CTC method than with the nalidixic acid method.

Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: Colony Count, Microbial--methods--MT; * **Enterobacter cloacae** -- **growth** and development--GD; *Water Microbiology; **Enterobacter cloacae** --isolation and purification--IP; Nalidixic Acid--pharmacology--PD; Tetrazolium Salts

CAS Registry No.: 0 (Tetrazolium Salts); 389-08-2 (Nalidixic Acid)

Record Date Created: 19950126

Record Date Completed: 19950126

4/9/12

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

08393047 95081026 PMID: 7989260

Survival of allochthonous bacteria in still mineral water bottled in polyvinyl chloride (PVC) and glass.

Moreira L; Agostinho P; Morais P V; da Costa M S

Departamento de Bioquimica, Instituto de Investigacao da Agua, Universidade de Coimbra, Portugal.

Journal of applied bacteriology (ENGLAND) Sep 1994, 77 (3) p334-9,

ISSN 0021-8847 Journal Code: 7503050
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The mortality of Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae and Pseudomonas aeruginosa, based on the **culturability** of these bacteria, was assessed in non-carbonated mineral water, bottled in polyvinyl chloride (PVC) containing the indigenous flora, sterile mineral water bottled in PVC, sterile mineral water in glass containers, and sterile tap water in glass containers. There was a general decrease in the **culturability** of these organisms in the four test waters, except that Ps. aeruginosa grew in sterile tap water. Escherichia coli and Kl. pneumoniae had the highest mortality rates under the conditions tested, while Ent. cloacae had a very low and constant mortality rate that would have resulted in the persistence of this organism in mineral water for a long period of time. After a sharp initial decrease in **culturability** , Ps. aeruginosa also had a very low mortality rate in mineral water bottled in PVC.

Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Descriptors: **Enterobacter cloacae** -- **growth** and development--GD; *Escherichia coli-- **growth** and development--GD; *Klebsiella pneumoniae-- **growth** and development--GD; *Pseudomonas aeruginosa-- **growth** and development--GD; *Water Microbiology; *Water Supply; Glass; Polyvinyl Chloride

CAS Registry No.: 0 (Glass); 9002-86-2 (Polyvinyl Chloride)
Record Date Created: 19950109
Record Date Completed: 19950109

4/9/13
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08393045 95081024 PMID: 7989258

Resistance of bacterial strains to dry conditions: use of anhydrous silica gel in a desiccation model system.

Janning B; in 't Veld P H; Notermans S; Kramer J
National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

Journal of applied bacteriology (ENGLAND) Sep 1994, 77 (3) p319-24,
ISSN 0021-8847 Journal Code: 7503050
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The viability of 18 bacterial strains desiccated on anhydrous silica gel and stored at a temperature of 22 degrees C for at least 3 months was determined. According to their stability in the dried state, these strains could be classified into three typical groups. Group 1, containing Gram-positive strains and Salmonella serotypes, was marked by a very slow decrease of the concentration of **culturable** cells from day 14 on (respectively day 21 for Salmonella thompson). The rate of decrease expressed as regression coefficient (b) ranged from -0.000389 to -0.00521 log (cfp ml-1) per d. The Group 2 strains Enterobacter cloacae and Escherichia coli did not reach a comparable slow decrease in the dry material within the indicated time period. Regression coefficients were respectively -0.04406 and -0.03412 log (cfp ml-1) per d. The reciprocal values -(1/b) were respectively 23 d per log (cfp ml-1) and 29 d per log (cfp ml-1), indicating the time periods in which a reduction of 1 log unit of **culturable** cells occurred. Group 3 strains Pseudomonas aeruginosa, Aeromonas hydrophila and Aer. sobria were marked by a significant susceptibility to cell damage caused during desiccation and reconstitution. A high initial decrease (ID) of the concentration of **culturable** organisms seems to be a characteristic property of these bacterial strains: **culturable** organisms could not be detected after storage for 1 d (Aer. hydrophila, Aer. sobria) or 7 d (Ps. aeruginosa). The wide range of resistance of the different bacterial strains tested indicated that the

silica gel model system is a suitable tool for microbiological challenge tests to investigate the survival of micro-organisms exposed to desiccation and their stability in dry materials.
Tags: Comparative Study
Descriptors: Acclimatization; *Gram-Negative Bacteria-- **growth** and development--GD; *Gram-Positive Bacteria-- **growth** and development--GD; Aeromonas-- **growth** and development--GD; Desiccation; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli-- **growth** and development --GD; Pseudomonas aeruginosa-- **growth** and development--GD; Salmonella-- **growth** and development--GD; Species Specificity; Time Factors
Record Date Created: 19950109
Record Date Completed: 19950109

4/9/14
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08284492 94350730 PMID: 8071132
Combination effect of clindamycin with ceftazidime and cefoperazone in inducing filamentous growth **of Enterobacter cloacae and Pseudomonas aeruginosa.**
Nishihata T; Kunieda S; Mikawa M; Nakahama C; Soejima R
Upjohn Tsukuba Research Laboratories, Ibaraki, Japan.
Journal of antibiotics (JAPAN) Jul 1994, 47 (7) p843-7, ISSN 0021-8820 Journal Code: 0151115
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Descriptors: Antibiotics, Combined--pharmacology--PD; *Enterobacter cloacae--drug effects--DE; * **Enterobacter cloacae** -- **growth** and development--GD; *Pseudomonas aeruginosa--drug effects--DE; *Pseudomonas aeruginosa-- **growth** and development--GD; Cefoperazone--pharmacology--PD; Ceftazidime--pharmacology--PD; Clindamycin--pharmacology--PD; Microbial Sensitivity Tests
CAS Registry No.: 0 (Antibiotics, Combined); 18323-44-9 (Clindamycin) ; 62893-19-0 (Cefoperazone); 78439-06-2 (Ceftazidime)
Record Date Created: 19940927
Record Date Completed: 19940927

4/9/15
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08216746 94282688 PMID: 8012906
The energy dependence of detergent resistance in Enterobacter cloacae: a likely requirement for ATP rather than a proton gradient or a membrane potential.
Aspedon A; Nickerson K W
School of Biological Sciences, University of Nebraska, Lincoln 68588-0343.
Canadian journal of microbiology (CANADA) Mar 1994, 40 (3) p184-91, ISSN 0008-4166 Journal Code: 0372707
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The enteric bacterium Enterobacter cloacae was **grown** both aerobically and anaerobically in the presence of up to 1% of the anionic detergent sodium dodecyl sulfate (SDS). A continuous energy supply was necessary to maintain cell integrity and cells **grown** in SDS (0.1-1%) lysed during carbon-limited stationary phase. The respiratory inhibitor KCN (3 mM) caused rapid lysis when added to aerobic, log phase, SDS-containing **cultures growing** on glucose as the carbon source. However, when the SDS (0.5%) was added 30 min after KCN, lysis did not occur. The likely reason

SYSTEM:OS - DIALOG OneSearch
File 155:MEDLINE(R) 1966-2004/Jan W2
(c) format only 2004 The Dialog Corp.
*File 155: Medline is updating again (12-22-2003).
Please see HELP NEWS 154, for details.
File 5:Biosis Previews(R) 1969-2004/Jan W1
(c) 2004 BIOSIS
File 73:EMBASE 1974-2004/Jan W1
(c) 2004 Elsevier Science B.V.
*File 73: New prices as of 1-1-04 per information provider request. See ?RATES 73

Set	Items	Description

Cost is in DialUnits
?ds

Set	Items	Description
S1	1736	CLOACAE?/TI AND ENTEROBACTER?/TI
S2	934	RD (unique items)
S3	258	S2/1998:2003
S4	676	S2 NOT S3
S5	2	S3 AND RECOMBIN? AND CULTUR?
S6	11	S4 AND RECOMBIN?

?t s6/9/all

6/9/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10797137 97086631 PMID: 8932320
Sequence and properties of pentaerythritol tetranitrate reductase from Enterobacter cloacae **PB2.**
French C E; Nicklin S; Bruce N C
Institute of Biotechnology, University of Cambridge, United Kingdom.
Journal of bacteriology (UNITED STATES) Nov 1996, 178 (22) p6623-7, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Pentaerythritol tetranitrate reductase, which reductively liberates nitrite from nitrate esters, is related to old yellow enzyme. Pentaerythritol tetranitrate reductase follows a ping-pong mechanism with competitive substrate inhibition by NADPH, is strongly inhibited by steroids, and is capable of reducing the unsaturated bond of 2-cyclohexen-1-one.
Descriptors: *Enterobacter cloacae--genetics--GE; *Oxidoreductases --genetics--GE; *Oxidoreductases--metabolism--ME; Amino Acid Sequence; Base Sequence; Cloning, Molecular; Cyclohexanones--metabolism--ME; Enterobacter cloacae--enzymology--EN; Kinetics; Models, Chemical; Molecular Sequence Data; NADP--metabolism--ME; Nitroglycerin--metabolism--ME; Oxidation-Reduction; Oxidoreductases--antagonists and inhibitors--AI; **Recombinant** Proteins--biosynthesis--BI; Sequence Analysis, DNA; Sequence Homology, Amino Acid; Testosterone--pharmacology--PD
Molecular Sequence Databank No.: GENBANK/U68759
CAS Registry No.: 0 (Cyclohexanones); 0 (Recombinant Proteins); 53-59-8 (NADP); 55-63-0 (Nitroglycerin); 57-85-2 (Testosterone); 930-68-7 (2-cyclohexen-1-one)
Enzyme No.: EC 1. (Oxidoreductases); EC 1.7.99.- (pentaerythritol tetranitrate reductase)
Record Date Created: 19970107
Record Date Completed: 19970107

6/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

10561307 96373189 PMID: 8776890
Crystallization and preliminary X-ray diffraction analysis of UDP-N-acetylglucosamine enolpyruvyltransferase of Enterobacter cloacae .

Sack S; Dauter Z; Wanke C; Amrhein N; Mandelkow E; Schonbrunn E
Max-Planck-Unit for Structural Molecular Biology, Hamburg, Germany.
Journal of structural biology (UNITED STATES) Jul-Aug 1996, 117 (1) p73-6, ISSN 1047-8477 Journal Code: 9011206
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Single crystals of UDP-N-acetylglucosamine enolpyruvyltransferase of Enterobacter cloacae have been grown by vapor diffusion using phosphate buffer as the precipitant. The crystals belong to the monoclinic space group C2 with a = 86.9 A, b = 155.9 A, c = 83.8 A, beta = 91.6 degrees. Assuming two monomers per asymmetric unit, the solvent content of these crystals is 63%. Flash-frozen crystals diffract to beyond 2 A resolution.
Descriptors: *Enterobacter cloacae--enzymology--EN; *Transferases --chemistry--CH; Crystallization; Crystallography, X-Ray; Protein Conformation; **Recombinant** Proteins--chemistry--CH
CAS Registry No.: 0 (Recombinant Proteins)
Enzyme No.: EC 2. (Transferases); EC 2.5.1.7 (UDP-N-acetylglucosamine 1-carboxyvinyltransferase)
Record Date Created: 19970508
Record Date Completed: 19970508

6/9/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08161175 94227050 PMID: 8172894
Role of residue Lys315 in the mechanism of action of the Enterobacter cloacae **908R beta-lactamase.**
Monnaie D; Dubus A; Cooke D; Marchand-Brynaert J; Normark S; Frere J M
Centre d'Ingenierie des Proteines, Universite de Liege, Belgium.
Biochemistry (UNITED STATES) May 3 1994, 33 (17) p5193-201, ISSN 0006-2960 Journal Code: 0370623
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The role of the highly conserved Lys315 residue in the catalytic mechanism of a class C beta-lactamase has been probed by site-directed mutagenesis. Lys315 has been replaced by a histidine in the Enterobacter cloacae 908R beta-lactamase, thus introducing a tritratable group to probe the role of the positive charge, and by a glutamine. The effects of these mutations have been studied on the kinetics of penicillin G and cephalothin turnover and on the pre-steady-state kinetics with carbenicillin at different pH. Results showed that substrate binding was not impaired by the mutations, so that an interaction with the substrate-free carboxylate in the Henri-Michaelis complex could be ruled out. Lys315 must have a catalytic role as shown by the decreased acylation and deacylation rates observed with the mutant enzymes. The mutants exhibited a lower activity at acidic pH, and this observation could be correlated with a decreased affinity for (3-aminophenyl)boronate, a compound devoid of free carboxylate which binds to the active site and forms an adduct mimicking the tetrahedral intermediate. This suggested that Lys315 was somehow involved in accelerating the nucleophilic substitutions along the reaction pathway. The study was extended to modified substrates where the free carboxylate had been esterified. Neither acylation nor deacylation seemed severely impaired with these compounds, showing that the interaction between the enzyme and the substrate-free carboxylate did not play a major role in catalysis.
Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: *Enterobacter cloacae--enzymology--EN; *Lysine; *beta-Lactamases--chemistry--CH; *beta-Lactamases--metabolism--ME; Amino Acid Sequence; Base Sequence; Conserved Sequence; Escherichia coli; Histidine; Hydrogen-Ion Concentration; Kinetics; Magnetic Resonance Spectroscopy; Molecular Sequence Data; Mutagenesis, Site-Directed; Oligodeoxyribonucleotides; Penicillins--chemical synthesis--CS; Penicillins--metabolism--ME; Plasmids; **Recombinant** Proteins--biosynthesis--BI; **Recombinant** Proteins--chemistry--CH; **Recombinant** Proteins--metabolism--ME; Spectrophotometry, Infrared; Substrate Specificity; beta-Lactamases--biosynthesis--BI

CAS Registry No.: 0 (Oligodeoxyribonucleotides); 0 (Penicillins); 0 (Plasmids); 0 (Recombinant Proteins); 56-87-1 (Lysine); 71-00-1 (Histidine)

Enzyme No.: EC 3.5.2.6 (beta-Lactamases)

Record Date Created: 19940608

Record Date Completed: 19940608

6/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

07842310 93297955 PMID: 8517720

Biochemical properties of a carbapenem-hydrolyzing beta-lactamase from Enterobacter cloacae and cloning of the gene into Escherichia coli.

Nordmann P; Mariotte S; Naas T; Labia R; Nicolas M H

Laboratoire de Microbiologie, Hopital Raymond Poincare, Faculte de Medecine Paris-Ouest, Garches, France.

Antimicrobial agents and chemotherapy (UNITED STATES) May 1993, 37 (5) p939-46, ISSN 0066-4804 Journal Code: 0315061

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A clinical isolate of Enterobacter cloacae, strain NOR-1, exhibited resistance to imipenem and remained susceptible to extended-spectrum cephalosporins. Clavulanic acid partially restored the susceptibility of the strain to imipenem. Two beta-lactamases with isoelectric points (pI) of 6.9 and > 9.2 were detected in strain E. cloacae NOR-1; the higher pI corresponded to AmpC cephalosporinase. Plasmid DNA was not detected in E. cloacae NOR-1 and imipenem resistance could not be transferred into Escherichia coli JM109. The carbapenem-hydrolyzing beta-lactamase gene was cloned into plasmid pACYC184. One **recombinant** plasmid, pPTN1, harbored a 5.3-kb Sau3A fragment from E. cloacae NOR-1 expressing the carbapenem-hydrolyzing beta-lactamase. This enzyme (pI 6.9) hydrolyzed ampicillin, cephalothin, and imipenem more rapidly than it did meropenem and aztreonam, but it hydrolyzed extended-spectrum cephalosporins only weakly and did not hydrolyze cefoxitin. Hydrolytic activity was partially inhibited by clavulanic acid, sulbactam, and tazobactam, was nonsusceptible to chelating agents such as EDTA and 1,10-o-phenanthroline, and was independent of the presence of ZnCl2. Its relative molecular mass was 30,000 Da. Induction experiments concluded that the carbapenem-hydrolyzing beta-lactamase biosynthesis was inducible by cefoxitin and imipenem. Subcloning experiments with HindIII partial digests of pPTN1 resulted in a **recombinant** plasmid, designated pPTN2, which contained a 1.3-kb insert from pPTN1 and which conferred resistance to beta-lactam antibiotics.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Support, Non-U.S. Gov't

Descriptors: *Carbapenems--metabolism--ME; *Enterobacter cloacae--enzymology--EN; *Enterobacter cloacae--genetics--GE; *Escherichia coli--enzymology--EN; *Escherichia coli--genetics--GE; *Genes, Bacterial; *beta-Lactamases--genetics--GE; Cloning, Molecular; DNA, Bacterial--chemistry--CH; Drug Resistance, Microbial; Hydrolysis; Isoelectric Focusing; Microbial Sensitivity Tests; Molecular Weight; Nucleic Acid Hybridization; Sequence Homology, Nucleic Acid; beta-Lactamases--biosynthesis--BI

CAS Registry No.: 0 (Carbapenems); 0 (DNA, Bacterial)

Enzyme No.: EC 3.5.2.6 (beta-Lactamases)

Record Date Created: 19930722
Record Date Completed: 19930722

6/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07484890 92348448 PMID: 1639814
Purification and characterization of indolepyruvate decarboxylase. A novel enzyme for indole-3-acetic acid biosynthesis in Enterobacter cloacae .
Koga J; Adachi T; Hidaka H
Bio Science Laboratories, Meiji Seika Kaisha, Ltd., Saitama, Japan.
Journal of biological chemistry (UNITED STATES) Aug 5 1992, 267 (22) p15823-8, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Indolepyruvate decarboxylase, a key enzyme for indole-3-acetic acid biosynthesis, was found in extracts of Enterobacter cloacae. The enzyme catalyzes the decarboxylation of indole-3-pyruvic acid to yield indole-3-acetaldehyde and carbon dioxide. The enzyme was purified to apparent homogeneity from Escherichia coli cells harboring the genetic locus for this enzyme obtained from E. cloacae. The results of gel filtration experiments showed that indolepyruvate decarboxylase is a tetramer with an M(r) of 240,000. In the absence of thiamine pyrophosphate and Mg2+, the active tetramers dissociate into inactive monomers and dimers. However, the addition of thiamine pyrophosphate and Mg2+ to the inactive monomers and dimers results in the formation of active tetramers. These results indicate that the thiamine pyrophosphate-Mg2+ complex functions in the formation of the tetramer, which is the enzymatically active holoenzyme. The enzyme exhibited decarboxylase activity with indole-3-pyruvic acid and pyruvic acid as substrates, but no decarboxylase activity was apparent with L-tryptophan, indole-3-lactic acid, beta-phenylpyruvic acid, oxalic acid, oxaloacetic acid, and acetoacetic acid. The Km values for indole-3-pyruvic acid and pyruvic acid were 15 microM and 2.5 mM, respectively. These results indicate that indole-3-acetic acid biosynthesis in E. cloacae is mediated by indolepyruvate decarboxylase, which has a high specificity and affinity for indole-3-pyruvic acid.
Descriptors: *Carboxy-Lyases--isolation and purification--IP; *Carboxy-Lyases--metabolism--ME; *Enterobacter cloacae--enzymology--EN; Carboxy-Lyases--genetics--GE; Chromatography, Ion Exchange; Cloning, Molecular; Electrophoresis, Polyacrylamide Gel; Enterobacter cloacae --genetics--GE; Escherichia coli--genetics--GE; Genes, Structural, Bacterial; Indoleacetic Acids--metabolism--ME; Kinetics; Macromolecular Systems; Magnesium Chloride--pharmacology--PD; Molecular Weight; **Recombinant** Proteins--isolation and purification--IP; **Recombinant** Proteins--metabolism--ME
CAS Registry No.: 0 (Indoleacetic Acids); 0 (Macromolecular Systems); 0 (Recombinant Proteins); 7786-30-3 (Magnesium Chloride); 87-51-4 (indoleacetic acid)
Enzyme No.: EC 4.1.1- (indolepyruvate decarboxylase); EC 4.1.1. (Carboxy-Lyases)
Record Date Created: 19920828
Record Date Completed: 19920828

6/9/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07001094 91241770 PMID: 2036007
Mobilization of the genetically engineered plasmid pHSV106 from Escherichia coli HB101(pHSV106) to Enterobacter cloacae **in drinking water.**

Sandt C H; Herson D S
School of Life and Health Sciences, University of Delaware, Newark 19716.
Applied and environmental microbiology (UNITED STATES) Jan 1991, 57 (1) p194-200, ISSN 0099-2240 Journal Code: 7605801
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

We have used triparental matings to demonstrate transfer (mobilization) of the nonconjugative genetically engineered plasmid pHSV106, which contains the thymidine kinase gene of herpes simplex virus cloned into pBR322, from Escherichia coli HB101 to an environmental isolate of Enterobacter cloacae in sterile drinking water. This is the first demonstration of a two-step mobilization of a genetically engineered plasmid in any type of fresh water, including drinking water. Transfer was mediated by R plasmid R100-1 of E. coli ED2149(R100-1). Matings in drinking water at 15, 25, and 35 degrees C yielded **recombinants** , the number of which increased with increasing temperature. Numbers of **recombinants** obtained were 2 orders of magnitude lower than those obtained from matings in Trypticase soy broth. High concentrations of parental organisms (2.6 x 10(8) to 2.0 x 10(9) CFU/ml) were required. During 1 week of incubation in drinking water, number of parental organisms and **recombinants** resulting from mobilization remained constant in the absence of indigenous organisms and declined in their presence. Using oligonucleotide probes for the cloned foreign DNA (thymidine kinase gene) and plasmid vector DNA (ampicillin resistance gene), we demonstrated that both genes were transferred to E. cloacae in the mobilization process. In one **recombinant** selected for detailed study, the plasmids containing these genes differed in size from all forms of pHSV106 present in E. coli HB101(pHSV106), indicating that DNA rearrangement had occurred. This **recombinant** maintained its plasmids in unchanged form for 15 days in drinking water. A second rearrangement occurred during serial passage of this **recombinant** on selective media.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Support, U.S. Gov't, Non-P.H.S.
Descriptors: *Enterobacter--genetics--GE; *Escherichia coli--genetics--GE ; *Plasmids; Cloning, Molecular; Gene Rearrangement; Genes, Bacterial; Genetic Engineering; Genetic Vectors; **Recombination** , Genetic; Transfection; Water Microbiology
CAS Registry No.: 0 (Genetic Vectors); 0 (Plasmids)
Record Date Created: 19910624
Record Date Completed: 19910624

6/9/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

06913892 91154203 PMID: 1999406
Cloning, nucleotide sequence, and expression of the nitroreductase gene from Enterobacter cloacae .
Bryant C; Hubbard L; McElroy W D
Department of Chemistry, University of California, San Diego, La Jolla 92093.
Journal of biological chemistry (UNITED STATES) Mar 5 1991, 266 (7) p4126-30, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The "classical" nitroreductases of enteric bacteria are flavoproteins which catalyze the reduction of a variety of nitroaromatic compounds to metabolites which are highly toxic, mutagenic, or carcinogenic. The gene for the nitroreductase Enterobacter cloacae has now been cloned using an antibody specific to this protein. The nucleotide sequence of the structural gene and flanking regions are reported. Sequence analysis indicates that this gene belongs to a gene family of flavoproteins which have not been previously described. Analysis of the 5'-untranslated region

reveals the presence of putative regulatory elements which may be involved in the modulation of the expression of this enzyme. The cloned gene was placed under the control of a T7 promoter for overexpression of the protein in Escherichia coli. The expressed **recombinant** protein was purified to homogeneity and exhibited physical, spectral, and catalytic properties identical to the protein isolated from E. cloacae.

Tags: Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Bacterial Proteins--genetics--GE; *Enterobacter--genetics --GE; *Genes, Structural, Bacterial; *Nitroreductases--genetics--GE; Amino Acid Sequence; Bacterial Proteins--immunology--IM; Bacterial Proteins --isolation and purification--IP; Base Sequence; Blotting, Western; Cloning, Molecular; DNA, Bacterial--genetics--GE; Enterobacter--enzymology --EN; Molecular Sequence Data; Molecular Weight; Restriction Mapping

Molecular Sequence Databank No.: GENBANK/M37085; GENBANK/M58580; GENBANK/M61895; GENBANK/M63808; GENBANK/M64255; GENBANK/M64256; GENBANK/M64257; GENBANK/M64258; GENBANK/M64259; GENBANK/M64260; GENBANK/M64485

CAS Registry No.: 0 (Bacterial Proteins); 0 (DNA, Bacterial)

Enzyme No.: EC 1.- (aromatic NADH-dependent nitroreductase); EC 1.7.- (Nitroreductases)

Record Date Created: 19910408

Record Date Completed: 19910408

6/9/8 (Item 8 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

06860191 91100276 PMID: 1987115

Molecular characterization of an Enterobacter cloacae **outer membrane protein (OmpX).**

Stoorvogel J; van Bussel M J; Tommassen J; van de Klundert J A

Department of Medical Microbiology, University Hospital, Leiden, The Netherlands.

Journal of bacteriology (UNITED STATES) Jan 1991, 173 (1) p156-60, ISSN 0021-9193 Journal Code: 2985120R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A chromosomal gene of Enterobacter cloacae encoding an outer membrane protein (OmpX) has been cloned. Overproduction of the OmpX protein decreased the quantity of porins in the outer membrane of the parental strain and of Escherichia coli HB101. The ompX gene was located by insertions of the gamma delta sequence into the **recombinant** plasmid. The polarity of the gene was determined by in vitro transcription and translation of the gamma delta-containing plasmids. The nucleotide sequence of the ompX gene was elucidated by using both inverted terminal repeats of the gamma delta sequence as starting points for M13 dideoxy sequencing. The gene was found to encode a precursor of the OmpX protein consisting of 172 amino acid residues with a molecular mass of 18.6 kDa. The protein contains an N-terminal signal sequence of 23 amino acid residues. The exact cleavage point was established by sequencing the N-terminal part of the mature protein. The OmpX protein has several characteristics in common with outer membrane proteins of gram-negative bacteria. The protein is rather hydrophilic and is devoid of long hydrophobic stretches. On the basis of these results, we present a model for the OmpX protein folding in an outer membrane.

Tags: Support, Non-U.S. Gov't

Descriptors: *Bacterial Outer Membrane Proteins--genetics--GE; *Enterobacter--genetics--GE; *Genes, Structural, Bacterial; Amino Acid Sequence; Base Sequence; Cell Membrane--ultrastructure--UL; Chromosomes, Bacterial; Cloning, Molecular; Escherichia coli--genetics--GE; Models, Molecular; Molecular Sequence Data; Plasmids; Protein Conformation; Restriction Mapping

Molecular Sequence Databank No.: GENBANK/M33878; GENBANK/M62909; GENBANK/M63621; GENBANK/M63622; GENBANK/M77223; GENBANK/S70358; GENBANK/S70359; GENBANK/S70363; GENBANK/S70365; GENBANK/S70370

CAS Registry No.: 0 (Bacterial Outer Membrane Proteins); 0 (Plasmids) ; 134632-13-6 (OmpX protein)
Record Date Created: 19910220
Record Date Completed: 19910220

6/9/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

05482992 87161784 PMID: 3030737
Inducible cephalosporinase production in clinical isolates of Enterobacter cloacae is controlled by a regulatory gene that has been deleted from Escherichia coli.
Honore N; Nicolas M H; Cole S T
EMBO journal (ENGLAND) Dec 20 1986, 5 (13) p3709-14, ISSN 0261-4189 Journal Code: 8208664
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Cephalosporin hyper-resistant Enterobacter cloacae strains are isolated with increasing frequency from hospital infections. Resistance is principally due to the chromosomal ampC gene encoding a cephalosporinase. In contrast to Escherichia coli which expresses ampC constitutively from a promoter located in the upstream frdD gene, E. cloacae displays inducible ampC expression. By cloning the ampC gene it was shown that a linked genetic locus, ampR, mediated the induction by beta-lactams. In the absence of the antibiotic the 30,500 dalton AmpR protein represses ampC expression. The ampR gene shows a highly compact arrangement and is situated between the divergently expressed ampC gene and the frd operon from which it is separated by a bifunctional transcription terminator. The promoters for ampR and ampC substantially overlap and mRNA analyses showed that on induction transcription from the ampC promoter increased greatly whereas that from ampR did not. Two regions of sequence homology flank the ampR gene and it is proposed that a homologous **recombination** event between these in an ancestral enteric bacterium may have led to the deletion of ampR from the E. coli genome.
Tags: Comparative Study; Human
Descriptors: *Cephalosporinase--genetics--GE; *Chromosome Deletion; *Enterobacter--genetics--GE; *Enterobacteriaceae--genetics--GE; *Escherichia coli--genetics--GE; *Genes, Bacterial; *Genes, Regulator; *Genes, Structural; *beta-Lactamases--genetics--GE; Base Sequence; Cephalosporinase --biosynthesis--BI; DNA Restriction Enzymes; Enterobacter--enzymology--EN; Enterobacter--isolation and purification--IP; Enzyme Induction; Escherichia coli--enzymology--EN; Sequence Homology, Nucleic Acid
Molecular Sequence Databank No.: GENBANK/X04730
Enzyme No.: EC 3.1.21 (DNA Restriction Enzymes); EC 3.5.2.- (Cephalosporinase); EC 3.5.2.6 (beta-Lactamases)
Record Date Created: 19870427
Record Date Completed: 19870427

6/9/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

00802689 70109411 PMID: 4905439
A bacteriocinogenic factor of Enterobacter cloacae .
Tieze G A; Stouthamer A H; Jansz H S; Zandberg J; van Bruggen E F
Molecular & general genetics - MGG (GERMANY, WEST) 1969, 106 (1) p48-65, ISSN 0026-8925 Journal Code: 0125036
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Descriptors: *Bacteriocins--biosynthesis--BI; *Enterobacter--metabolism

--ME; *Extrachromosomal Inheritance; Conjugation, Genetic; DNA, Bacterial --analysis--AN; DNA, Bacterial--isolation and purification--IP; Drug Resistance, Microbial; Escherichia coli--physiology--PH; Microscopy, Electron; **Recombination** , Genetic
CAS Registry No.: 0 (Bacteriocins); 0 (DNA, Bacterial)
Record Date Created: 19700326
Record Date Completed: 19700326

6/9/11 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2004 BIOSIS. All rts. reserv.

0008376149 BIOSIS NO.: 199294077990
MOLECULAR APPROACHES FOR UNDERSTANDING BIOLOGICAL CONTROL MECHANISMS IN BACTERIA STUDIES OF THE INTERACTION OF ENTEROBACTER - CLOACAE **WITH PYTHIUM-ULTIMUM**
AUTHOR: NELSON E B (Reprint); MALONEY A P
AUTHOR ADDRESS: DEP PLANT PATHOL, COLL AGRIC LIFE SCI, CORNELL UNIV, ITHACA, NY 14853, USA**USA
JOURNAL: Canadian Journal of Plant Pathology 14 (1): p106-114 1992
ISSN: 0706-0661
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Biocontrol activity represents a complex process that involves a series of events not unlike those involved in plant pathogenesis or in the establishment of symbiotic plant-microbe associations. This process can be thought of as a series of traits expressed synchronously or in a controlled sequence. Molecular biological techniques provide a means of experimentally isolating DNA sequences that control biocontrol phenotypes so that one can more definitively assess the role of biocontrol genes and their corresponding gene products in biocontrol processes. Since much of the basis for **recombinant** DNA technology has come from our understanding of bacterial genetics, molecular approaches are particularly suited for the study of bacterial-fungal biocontrol systems. A model biocontrol system involving the interaction of the bacterium Enterobacter cloacae with the seed rotting fungus Pythium ultimum is used to illustrate molecular approaches useful in the study of biocontrol processes. Enterobacterial traits such as exudate stimulant metabolism and adhesive properties and their role in the suppression of pythium seed rot are highlighted. Parallels with Escherichia coli physiology and genetics are discussed.

DESCRIPTORS: REVIEW ESCHERICHIA-COLI FUNGUS MICROORGANISM PHYSIOLOGY GENETICS CROP INDUSTRY AGRICULTURE
DESCRIPTORS:
MAJOR CONCEPTS: Genetics; Infection; Microbiology; Pest Assessment Control and Management; Physiology
BIOSYSTEMATIC NAMES: Enterobacteriaceae--Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Phycomycetes --Fungi, Plantae
COMMON TAXONOMIC TERMS: Bacteria; Eubacteria; Fungi; Microorganisms; Nonvascular Plants; Plants
CONCEPT CODES:
31000 Physiology and biochemistry of bacteria
31500 Genetics of bacteria and viruses
40000 Soil microbiology
54502 Phytopathology - Diseases caused by fungi
54516 Phytopathology - Disease control
BIOSYSTEMATIC CODES:
06702 Enterobacteriaceae
15900 Phycomycetes
?logoff hold
12jan04 11:46:56 User228206 Session D2103.18
$0.77 0.242 DialUnits File155
$2.10 10 Type(s) in Format 9
$2.10 10 Types

```
      $2.87  Estimated cost File155
             $0.27    0.048 DialUnits File5
                $1.75  1 Type(s) in Format  9
             $1.75  1 Types
      $2.02  Estimated cost File5
             $0.12    0.012 DialUnits File73
      $0.12  Estimated cost File73
             OneSearch, 3 files,  0.303 DialUnits FileOS
      $0.22  TELNET
      $5.23  Estimated cost this search
      $5.23  Estimated total session cost   0.303 DialUnits


### Status: Signed Off. (1 minutes)
```

02422480 Genuine Article#: LA017 Number of References: 42
Title: BIOCHEMICAL-PROPERTIES OF A CARBAPENEM-HYDROLYZING BETA-LACTAMASE FROM ENTEROBACTER- CLOACAE **AND CLONING OF THE GENE INTO ESCHERICHIA-COLI**
Author(s): NORDMANN P; MARIOTTE S; NAAS T; LABIA R; NICOLAS MH
Corporate Source: HOP RAY POINCARE,FAC MED PARIS OUEST,MICROBIOL LAB,104 BLVD RAYMOND POINCARE/F-92380 GARCHES//FRANCE/; HOP AMBROISE PARE,FAC MED PARIS OUEST,MICROBIOLLAB/F-92100 BOULOGNE//FRANCE/; MUSEUM HIST NAT,CNRS,URA 401/F-75231 PARIS 05//FRANCE/; UNIV BASEL,BIOZENTRUM,MIKROBIOL ABT/CH-4056 BASEL//SWITZERLAND/
Journal: ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, 1993, V37, N5 (MAY), P 939-946
ISSN: 0066-4804
Language: ENGLISH Document Type: ARTICLE
Geographic Location: FRANCE; SWITZERLAND
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: PHARMACOLOGY & PHARMACY; MICROBIOLOGY
Abstract: A clinical isolate of Enterobacter **cloacae** , **strain** NOR-1, exhibited resistance to imipenem and remained susceptible to extended-spectrum cephalosporins. Clavulanic acid partially restored the susceptibility of the **strain** to imipenem. Two beta-lactamases with isoelectric points (pI) of 6.9 and >9.2 were detected in **strain** E. **cloacae** NOR-1; the higher pI corresponded to AmpC cephalosporinase. Plasmid DNA was not detected in E. **cloacae** NOR-1 and imipenem resistance could not be transferred into Escherichia coli JM109. The carbapenem-hydrolyzing beta-lactamase gene was cloned into plasmid pACYC184. One **recombinant** plasmid, pPTN1, harbored a 5.3-kb Sau3A fragment from E. **cloacae** NOR-1 expressing the carbapenem-hydrolyzing beta-lactamase. This enzyme (pI 6.9) hydrolyzed ampicillin, cephalothin, and imipenem more rapidly than it did meropenem and aztreonam, but it hydrolyzed extended-spectrum cephalosporins only weakly and did not hydrolyze cefoxitin. Hydrolytic activity was partially inhibited by clavulanic acid, sulbactam, and tazobactam, was nonsusceptible to chelating agents such as EDTA and 1,10-o-phenanthroline, and was independent of the presence of ZnCl2. Its relative molecular mass was 30,000 Da. Induction experiments concluded that the carbapenem-hydrolyzing beta-lactamase biosynthesis was inducible by cefoxitin and imipenem. Subcloning experiments with HindIII partial digests of pPTN1 resulted in a **recombinant** plasmid, designated pPTN2, which contained a 1.3-kb insert from pPTN1 and which conferred resistance to beta-lactam antibiotics. Hybridization studies performed with a 1.2-kb HindIII fragment from pPTN2 failed to determine any homology with ampC of E. **cloacae** , with other known beta-lactamase genes commonly found in members of the family Enterobacteriaceae (bla(TEM-1) and blas(SHV-3) derivatives), and with previously described carbapenemase genes such as those from Xanthomonas maltophilia, Bacillus cereus, Bacteroides fragilis (cfiA), and Aeromonas hydrophila (cphA). This work describing the biochemical properties of a novel chromosome-encoded beta-lactamase from E. **cloacae** indicates that this enzyme differs from all the previously described carbapenemases. This is the first reported cloning of a carbapenem-hydrolyzing beta-lactamase gene from a member of the family Enterobacteriaceae.
Identifiers--KeyWords Plus: PSEUDOMONAS-AERUGINOSA; IMIPENEM RESISTANCE; BACTEROIDES-FRAGILIS; CEPHALOSPORINASE PRODUCTION; KLEBSIELLA-PNEUMONIAE; AEROMONAS-HYDROPHILA; CLINICAL ISOLATE; MALTOPHILIA; IDENTIFICATION; PURIFICATION
Research Fronts: 91-0102 002 (BETA-LACTAMASE INHIBITORS; NEWER ANTIMICROBIAL AGENTS; BACTEROIDES-FRAGILIS GROUP; INVITRO SUSCEPTIBILITY)
91-4817 002 (LIPASE GENE; CDNA FOR STIMULATORY GDP/GTP EXCHANGE **PROTEIN** ; EXPRESSION OF MESSENGER-RNA)
91-7435 002 (IMIPENEM RESISTANCE; OUTER-MEMBRANE **PROTEINS** OF CLINICAL XANTHOMONAS-MALTOPHILIA ISOLATES; BETA-LACTAM ANTIBIOTICS; INVITRO SUSCEPTIBILITY)
91-3898 001 (**GROWTH** OF ESCHERICHIA-COLI; PLASMID-ENCODED VIRULENCE GENE; INVIVO FUNCTION; MUTANT **STRAINS** ; POSITIVE REGULATOR)
Cited References:
BANDOH K, 1992, V45, P542, J ANTIBIOT
BARTHELEMY M, 1978, V13, P695, ANTIMICROBIAL AGENTS

BELLIDO F, 1990, V25, P57, J ANTIMICROB CHEMOTH
BICKNELL R, 1985, V229, P791, BIOCHEM J
BUSCHER KH, 1987, V31, P703, ANTIMICROB AGENTS CH
BUSH K, 1989, V33, P264, ANTIMICROBIAL AGENTS
CHANG ACY, 1978, V134, P1141, J BACTERIOL
CUCHURAL GJ, 1986, V30, P645, ANTIMICROB AGENTS CH
DUFRESNE J, 1988, V32, P819, ANTIMICROB AGENTS CH
FUJII T, 1986, V29, P925, ANTIMICROB AGENTS CH
GEHRLEIN M, 1991, V37, P405, CHEMOTHERAPY
HONORE N, 1986, V5, P3709, EMBO J
HURLBUT S, 1990, V34, P117, ANTIMICROB AGENTS CH
IACONIS JP, 1990, V34, P44, ANTIMICROB AGENTS CH
KADO CI, 1981, V145, P118, J BACTERIOL
LABIA R, 1981, V7, P49, J ANTIMICROB CHEMOTH
LEE EH, 1991, V35, P1093, ANTIMICROB AGENTS CH
LEVESQUE RC, 1987, V206, P252, MOL GEN GENET
LIM HM, 1978, V170, P2873, J BACTERIOL
LIVERMORE DM, 1992, V29, P609, J ANTIMICROB CHEMOTH
MANIATIS T, 1982, MOL CLONING
MASSIDDA O, 1991, V173, P4611, J BACTERIOL
MEDEIROS AA, 1986, 26TH INT C ANT AG CH
NICOLAS MH, 1987, V31, P295, ANTIMICROB AGENTS CH
NICOLAS MH, 1989, V33, P2096, ANTIMICROB AGENTS CH
NORDMANN P, 1990, 30TH INT SCI ANT AG
PETIT A, 1992, V29, P629, J ANTIMICROB CHEMOTH
PHILIPPON A, 1989, V33, P1131, ANTIMICROB AGENTS CH
PIERRE J, 1990, V34, P1695, ANTIMICROB AGENTS CH
PODGLAJEN I, 1992, V9, P21, FEMS MICROBIOL LETT
QUINN JP, 1986, V154, P289, J INFECT DIS
SAINO Y, 1982, V22, P564, ANTIMICROB AGENTS CH
SANDERS CC, 1992, V14, P1089, CLIN INFECT DIS
SATO K, 1985, V27, P612, ANTIMICROB AGENTS CH
SHANNON K, 1986, V17, P45, J ANTIMICROB CHEMOTH
SIROT D, 1987, V20, P323, J ANTIMICROB CHEMOTH
THOMPSON JS, 1990, V172, P2584, J BACTERIOL
TRIAS J, 1989, V33, P1201, ANTIMICROB AGENTS CH
WATANABE M, 1991, V35, P147, ANTIMICROB AGENTS CH
YANG YJ, 1990, V34, P755, ANTIMICROB AGENTS CH
YANISCHPERRON C, 1985, V33, P103, GENE
YOTSUJI A, 1983, V24, P925, ANTIMICROB AGENTS CH

Mechanisms of Disease: New Mechanisms Of Bacterial Resistance To Antimicrobial Agents (Review Article)

Jacoby, George A.; Archer, Gordon L.
The New England Journal of Medicine
Feb 28, 1991; 324 (9),pp 601-612
LINE COUNT: 00590 WORD COUNT: 08143
ISSN: 0028-4793
CORPORATE SOURCE: From the Infectious Disease Unit, Massachusetts General Hospital, Boston (G.A.J.), and the Division of Infectious Diseases, Medical College of Virginia, Virginia Commonwealth University, Richmond (G.L.A.). Address reprint requests to Dr. Jacoby at Massachusetts General Hospital, Boston, MA 02114. - Supported by grants (AI-20415 and AI-21772) from the National Institutes of Health.

TEXT

Sooner or later bacteria develop resistance to virtually any antimicrobial agent. Resistance has many consequences. The patient infected with a drug-resistant as opposed to a drug-sensitive organism is more likely to require hospitalization and have a longer hospital stay and has an increased risk of death (Ref. 1). Resistance also compels the use of more toxic or more expensive alternative drugs (Ref. 2). The unrecognized cost of antibiotic resistance in the United States has been estimated as at least $100 million annually (Ref. 3). Resistance thus affects the antibiotic options available to every practitioner and is no less a problem in the developing world (Ref. 4).

The evaluation of a new antimicrobial agent typically reveals some organisms that are naturally resistant and others that appear to be susceptible, thus defining the spectrum of activity for that agent. Laboratory tests can estimate the likelihood that resistance will develop, but often the important mechanisms for resistance emerge only with clinical use. Despite their versatility, bacteria have a limited number of mechanisms of acquired antimicrobial resistance, including a change in the drug target, the production of a detoxifying enzyme, or decreased antibiotic uptake (Table 1). Alterations in the target include both reduction of receptor affinity and the substitution of an alternative pathway, whereas decreased uptake may occur through either diminished permeability or an active efflux system. Furthermore, a resistant organism may use more than one of these strategies. Diminished accumulation, for example, can augment the other resistance mechanisms synergistically.
*Table 1. Major Mechanisms of Resistance to Antimicrobial Agents *. **TABLE OMITTED**

Resistance may arise by a mutation that reduces target affinity or allows the overproduction of a drug-modifying enzyme. Sometimes the insertion of foreign DNA by recombination accomplishes the same end. More often resistance genes are carried on extrachromosomal plasmids that may be transferable from organism to organism by conjugation, transduction, or transformation (Ref. 21). The genes may even be packaged in units of DNA called transposons that allow them to jump from one DNA site to another, thus further facilitating the spread of resistance.

The topic of bacterial resistance to antibiotics has been reviewed periodically (Ref. 22-25). This article will focus on new resistance mechanisms that have appeared in response to the widespread use of newer, broad-spectrum antibiotics and the increased and often indiscriminate use of older agents. Novel mechanisms have appeared, as well as alterations of old mechanisms to mediate resistance to new antimicrobial agents. Old resistance genes have been acquired by new hosts, and some bacteria have accumulated resistance to a multiplicity of antimicrobial agents. Only drugs currently available commercially in the United States will be considered. Ultimately, knowledge of how resistance to antimicrobial agents develops should aid in limiting the evolution and spread of resistant pathogens.

Resistance to Broad-Spectrum beta-Lactam Antibiotics in Gram-Negative Organisms

The development of new beta-lactam antibiotics has been inspired by the success of bacteria in developing resistance to the older ones. Thus, just as semisynthetic penicillins such as methicillin, oxacillin, and nafcillin were perfected to overcome penicillinase-producing Staphylococcus aureus, broad-spectrum cephalosporins, carbapenems, and monocyclic

beta-lactam antibiotics (monobactams) were developed to deal with beta-lactamase-producing gram-negative pathogens that were resistant to ampicillin, carbenicillin, piperacillin, or ticarcillin (Table 2). *Table 2. Characteristics of Broad-Spectrum Resistance to b-Lactam Antibiotics *. **TABLE OMITTED**

Bacteria have met this challenge in various ways. Virtually all gram-negative bacteria have a chromosomal gene for beta-lactamase called ampC that encodes an enzyme more active in hydrolyzing cephalosporins than penicillins. In enterobacter species, serratia species, indole-positive proteus species, Citrobacter freundii, Pseudomonas aeruginosa, and a few other organisms, additional genes regulate the production of this beta-lactamase. These bacteria can undergo single-step mutations to constitutive, high-level enzyme production (Ref. 26). Even though the AmpC enzyme hydrolyzes broad-spectrum cephalosporins poorly, if enough AmpC beta-lactamase is made, resistance results (Ref. 27,28). Consequently, initially susceptible **strains** of Enterobacter **cloacae** and other organisms in which beta-lactamase production can be induced have become resistant during therapy with broad-spectrum cephalosporins at rates in the range of 10 to 20 percent (Ref. 29The chromosomal beta-lactamase of Escherichia coli is not inducible and normally is made in such low amounts that it does not contribute appreciably to beta-lactam resistance. However, clinical **strains** resistant to ampicillin and cephalosporins have been isolated that make large amounts of chromosomal enzyme because the promoter for ampC has been altered to allow more efficient expression. In several isolates this strong promoter resembles that normally found in shigella species changed by a single nucleotide, so that these Esch. coli appear to owe their resistance to a regulatory element from another genus taking over beta-lactamase production (Ref. 30).

In most gram-negative organisms beta-lactam resistance results from a plasmid-mediated beta-lactamase. More than 30 varieties can be distinguished on the basis of biochemical criteria such as the substrate profile and isoelectric point, but by far the most common plasmid-encoded enzyme is TEM-1; SHV-1 is also frequent in Klebsiella pneumoniae, and PSE-1 is the most common variety on plasmids in P. aeruginosa (Ref. 14). These enzymes confer resistance to ampicillin, carenicillin, ticarcillin, cephalothin, and cefamandole but not to broad-spectrum cephalosporins, monobactams, or cephamycins. Consequently, it was unexpected when plasmid-mediated resistance to expanded-spectrum beta-lactam antibiotics was reported from Europe in 1983 (Ref. 31) and was shown to result from an extended-spectrum beta-lactamase (Ref. 32). Subsequently, plasmid-mediated beta-lactamases with extended spectrums have been reported from around the world (Ref. 33,34) in a variety of gram-negative pathogens, but especially in K. pneumoniae. The enzymes provide resistance to oxyimino-beta-lactams such as cefotaxime, ceftazidime, ceftriaxone, and aztreonam (a monobactam) (Ref. 35). Some are related to TEM-1, some to TEM-2 (a biochemical twin of TEM-1 except for one amino acid), and some to SHV-1. At least 16 varieties related to TEM (Ref. 36) and 4 related to SHV have been distinguished. The extended-spectrum beta-lactamases differ from their progenitors by one, two, or three amino acid substitutions that alter the configuration around a serine at the active site of the enzyme, thus increasing its affinity for broad-spectrum beta-lactam antibiotics. In the laboratory, similar mutant enzymes can be selected by exposure to broad-spectrum cephalosporins, (Ref. 32,37,38) making it likely that extended-spectrum beta-lactamases can emerge wherever antibiotic use favors their selection.

Strains producing a TEM-related or SHV-related beta-lactamase with an extended spectrum remain susceptible to cephamycins such as cefoxitin or cefotetan and to combination therapy with a beta-lactamase inhibitor, such as clavulanic acid or sulbactam. In fact, the ability of a disk containing one of these inhibitors to restore susceptibility near a disk containing aztreonam, cefotaxime, ceftazidime, or ceftriaxone provides an excellent screening test for the presence of this mechanism of resistance (Ref. 34). Recently, a third type of plasmid-mediated, extended-spectrum beta-lactamase has appeared. This enzyme provides resistance to beta-lactam antibiotics with a 7 alpha-methoxy group, such as cefoxitin, cefotetan, or moxalactam, as well as to oxyimino-beta-lactam antibiotics; it is not inhibited by clavulanic acid or sulbactam; and it is related not to SHV or TEM but to the AmpC beta-lactamase of Ent. **cloacae** (Ref. 39). How common this form of resistance will become remains to be seen.

All three types of extended-spectrum beta-lactamase are unable to

confer resistance to imipenem, (Ref. 35) but a few organisms produce specialized imipenem-hydrolyzing beta-lactamases, including rare isolates of Serratia marcescens, Ent. **cloacae** , and Bacteroides fragilis (Ref. 40,41)and virtually all **strains** of Xanthomonas (formerly Pseudomonas) maltophilia (Ref. 42). The responsible genes are chromosomal, which should limit the spread of such beta-lactamases to other bacteria. In a few organisms imipenem resistance has been associated with altered penicillin-binding **proteins** (Ref. 43,44). P. aeruginosa can also rather readily become resistant specifically to imipenem through the loss of an outer-membrane **protein** that provides a channel for the entry of imipenem, (Ref. 45) and a similar mechanism has been proposed for imipenem resistance in Ent. aerogenes (Ref. 46).

Methicillin Resistance in Staphylococci

In staphylococci beta-lactamase has shown much less apparent diversity, although some variation in substrate specificity has recently been recognized among the four long-known immunotypes of staphylococcal penicillinase (Ref. 47) and may have clinical importance (Ref. 48). The enzyme is normally inducible, but if produced constitutively at high levels, it has enough activity against some semisynthetic penicillins to cause borderline resistance in vitro to methicillin or particularly oxacillin (Ref. 49). This laboratory finding, however, seems not to be associated with therapeutic failures (Ref. 50,51).

True methicillin resistance has a different basis that involves the production of an enzyme able to maintain cell-wall integrity during **growth** and division when native enzymes (penicillin-binding **proteins**) needed for assembly of the cell wall are inactivated by beta-lactam antibiotics. In the typical methicillin-resistant **strain** of Staph. aureus the new drug-resistant target, termed penicillin-binding **protein** 2a (PBP 2a) or 2' (PBP 2'), mediates clinically relevant resistance to all beta-lactam antibiotics and is encoded by an acquired chromosomal gene (mecA) that is absent from organisms susceptible to methicillin. Identical mecA genes have been found in coagulase-positive and coagulase-negative staphylococci with the appropriate methicillin-resistant phenotype (Ref. 52). In a few Staph. aureus **strains** with a low level of resistance to methicillin, the mecA gene and PBP 2a are absent, but other penicillin-binding **proteins** are modified in beta-lactam reactivity (Ref. 53).

The spread of staphylococcal clones carrying the PBP 2a gene or the horizontal transfer of the gene itself has resulted in the worldwide dissemination of methicillin-resistant staphylococci (Ref. 54,55). In the United States, methicillin-resistant **strains** of Staph. aureus are no longer present only in the large tertiary care teaching hospitals that were once their predominant province but have moved into large and small non-teaching hospitals and into community nursing homes (Ref. 56,57). They now represent approximately 15 percent of all nosocomial Staph. aureus isolates (Ref. 58). The prevalence of resistance among nosocomial coagulase-negative staphylococci is even higher: 75 percent of Staph. epidermidis **strains** and 80 percent of Staph. haemolyticus **strains** are resistant, according to recent surveys (Ref. 58,59).

The expression of beta-lactam resistance mediated by PBP 2a varies remarkably. Homogeneous **strains** express resistance uniformly in every member of the population, whereas in heterogeneous **strains** only 1 in 10(sup 3) to 10(sup 6) cells of a **culture** expresses resistance. Three genetic systems have been described that influence the expression of mecA or its gene product. First, it has been observed that the production of PBP 2a is induced by beta-lactam antibiotics when the cell contains both the mecA gene and a plasmid carrying genes for the inducible production of penicillinase (Ref. 60). Sequencing has revealed that the promoter regions of the mecA and penicillinase genes are similar, accounting for the coordinate regulation of their genes (Ref. 61). However, although the amount of PBP 2a is clearly subject to induction in the presence of penicillinase-regulatory genes, it is not clear that the quantity of PBP 2a is related to the homogeneous or heterogeneous expression of resistance (Ref. 62). The second gene related to the expression of methicillin resistance has been called femA (Ref. 63). When this gene was inactivated in a typical heterogeneously resistant **strain** , the susceptible population of cells increased 1000-fold (Ref. 64). The femA gene is far removed from mecA and has no effect on the level of PBP 2a production. The mechanism by which its gene product influences the expression of methicillin resistance is unknown. A third regulatory system has recently been found in Staph.

epidermidis (Ref. 65). Sequences just upstream from mecA in a highly heterogeneous clinical isolate appear to repress the expression of PBP 2a. When these sequences were deleted, both PBP 2a expression and the level of resistance increased. These sequences were not related to the penicillinase-regulatory genes described above.

Heterotypical expression of resistance is a particularly vexing problem because such resistant staphylococci are often difficult to detect in the clinical-microbiology laboratory yet appear to be as resistant to treatment with beta-lactam antibiotics as their homogeneous counterparts (reviewed by Chambers (Ref. 66)). Detection systems based on identifying the mecA gene or gene products might be preferable to many of the phenotype-based tests, particularly those used in rapid, automated systems (Ref. 67). The relations among the phenotypic expression of methicillin resistance, the quantity of PBP 2a, and the additional genes affecting the expression of resistance are clearly complex and must be elucidated before a complete understanding of the nature of methicillin resistance can be achieved.

Low-Affinity Penicillin-Binding **Proteins** as a Resistance Mechanism in Other Organisms

The mecA gene is confined to staphylococci, but other organisms also produce low-affinity penicillin-binding **proteins** as a mechanism of resistance to beta-lactam antibiotics. The uniformly poor activity of beta-lactam antibiotics against enterococci is the result of a low-affinity penicillin-binding **protein** (Ref. 68). Penicillin-resistant pneumococci have several penicillin-binding **proteins** with decreased penicillin-binding affinity, and each contributes incrementally to resistance (Ref. 69). Sequencing studies have shown that a resistant penicillin-binding **protein** gene is so different from that found in penicillin-sensitive pneumococci that it could not have arisen by mutation. The gene has a mosaic structure with segments similar to those of a sensitive penicillin-binding **protein** alternating with segments that must have come from another organism, presumably another type of streptococcus (Ref. 70). Penicillin-resistant pneumococci are found in the United States, but their prevalence is still low (Ref. 71). Although resistance is usually slight (minimal inhibitory concentration, 0.1 to 2.0 microg per milliliter), it is sufficient to produce penicillin treatment failures in cases of meningitis (Ref. 72). Higher levels of resistance (minimal inhibitory concentration, 2.0 to 8.0 microg per milliliter) have been associated with the failure of therapy for pneumonia and bacteremia (Ref. 73). As a result, general testing of pneumococci for susceptibility to penicillin is now recommended (Ref. 74).

Altered penicillin-binding **proteins** have also been reported in clinical isolates of Haemophilus influenzae, (Ref. 75) Neisseria gonorrhoeae, (Ref. 76) and N. meningitidis that were resistant to penicillin or ampicillin and did not produce beta-lactamase (Ref. 77). As with the pneumococcus, the PBP 2 gene of the resistant meningococcus is a mosaic of segments similar to the gene from a sensitive **strain** and segments identical to those of a commensal neisseria species (Ref. 78). The PBP 2 gene of a resistant gonococcus has a similar hybrid structure (Ref. 79). It seems more than coincidental that the bacteria demonstrating such **recombinant** genes for penicillin-binding **proteins** are naturally transformable and so can acquire homologous DNA from related species (Ref. 79).

Transmissible Resistance to Vancomycin

Vancomycin has become the mainstay of parenteral therapy for gram-positive bacteria resistant to beta-lactam antibiotics and for patients allergic to beta-lactam antibiotics. The increasing prevalence of methicillin-resistant staphylococci was followed by a remarkable increase in the use of vancomycin by hospitals. Resistance to vancomycin had not been described since its introduction in the 1960s, but with increased use, reports of vancomycin resistance began to appear. First, infections with commensal bacteria naturally resistant to the antibiotic, such as leuconostoc, (Ref. 80) lactobacillus, (Ref. 81) and Staph. haemolyticus, (Ref. 82) were described. However, a report from France in 1988 (Ref. 83) that a bacterium, Enterococcus faecium, was resistant to vancomycin by virtue of a gene (vanA) carried on a transmissible plasmid was especially disturbing. Fortunately, the plasmid encoding vancomycin resistance could not be transferred to Staph. aureus, but it could be transmitted to other streptococci. Subsequently, additional vancomycin-resistance genes were

found in Enterococcus faecalis (Ref. 84).

Vancomycin blocks the synthesis of bacterial cell walls by binding to the d-alanyl-d-alanine terminus of the peptidoglycan stem peptide (Ref. 85). Resistance to vancomycin is associated with the production of a new membrane-associated **protein** of 39 to 40 kd that competitively inhibits this binding (Ref. 12). The **protein** appears to act as a carboxypeptidase to remove the terminal d-Ala from the pentapeptide, thus preventing access of vancomycin to its target. Although initially seen in France and England, (Ref. 86) vancomycin-resistant enterococci have since been found in the United States (Ref. 87). Whether or not a similar resistance gene has the potential for conferring vancomycin resistance on methicillin-resistant **strains** of Staph. aureus has not yet been established.

Resistance to Amikacin

Amikacin, a semisynthetic derivative of kanamycin, was designed to be a poor substrate for many of the modifying enzymes that attack gentamicin, tobramycin, or its parent, kanamycin. Hence, amikacin has been effective against many clinical isolates resistant to other aminoglycosides. When it has been used as the predominant aminoglycoside, the level of amikacin resistance has remained low in some hospitals (Ref. 88-90) but has increased in others (Ref. 91-93). When resistance to amikacin has increased, one of the mechanisms listed in Table 3 has been involved. Some gram-negative organisms, especially P. aeruginosa, can become resistant to amikacin by nonenzymatic mechanisms that decrease the general uptake of aminoglycosides, (Ref. 94) such as those altering energy metabolism (Ref. 101) or the lipopolysaccharide structure of the cell wall (Ref. 102). Other organisms rely on enzymatic modification, which is usually encoded by plasmids and hence potentially transmissible. In gram-negative pathogens the 6'-acetyltransferase mechanism is the most common and is determined by at least two gene types (Ref. 103). Several 3'-phosphotransferases can provide amikacin resistance, (Ref. 92,95,96) whereas a 4'-nucleotidyltransferase that modifies amikacin is a new addition to the gram-negative resistance repertoire (Ref. 93). *Table 3Mechanisms of Amikacin Resistance *. **TABLE OMITTED**

Aminoglycoside Resistance in Gram-Positive Cocci

In staphylococci, resistance to gentamicin, the most widely used antistaphylococcal aminoglycoside, is mediated almost exclusively by enzyme modification. The bifunctional 6'-acetylating and 2''-phosphorylating enzyme (Table 3) is the most common. Resistance to amikacin, kanamycin, and tobramycin is mediated by the domain having 6'-acetylating activity, whereas resistance to gentamicin results from the 2''-phosphorylating activity toward the carboxy terminal of the **protein** (Ref. 104). Homologous genes encoding this activity have been found in Staph. aureus and many different species of coagulase-negative staphylococci, encoded by both plasmids and transposable DNA elements (Ref. 59,105,106). Plasmids carrying this gene have been shown to move among staphylococcal species by conjugation and may be partially responsible for the rapid increase in gentamicin resistance among staphylococci in the United States during the past decade (Ref. 107,108). Additional, different aminoglycoside-modifying enzymes that mediate resistance to streptomycin, neomycin, and amikacin have been found in staphylococci, but they are less prevalent and of less clinical importance (Ref. 109).

Enterococci are naturally resistant to clinically achievable concentrations of streptomycin or gentamicin, but the addition of some beta-lactam antibiotics allows entry of the aminoglycoside into the cell and produces a synergistic combination that results in cell death. Enterococci that are highly resistant to gentamicin by virtue of plasmid-mediated enzymes that inactivate aminoglycosides were first reported in 1979 and have become more common over the past decade (reviewed by Patterson and Zervos (Ref. 110)). These isolates are resistant to synergistic killing by beta-lactam and aminoglycoside antibiotics. Outbreaks have been described in which more than 50 percent of the enterococcal isolates from some hospitals were resistant to aminoglycosides (Ref. 110). The most prevalent enterococcal gene for gentamicin resistance is homologous to the bifunctional 6'-acetylating and 2''-phosphorylating enzyme of Staph. aureus. Its prevalence may be due to its location on both a highly efficient conjugative plasmid and a mobile genetic element (Ref. 111).

Resistance to Fluoroquinolones

Bacteria can mutate to become resistant to ciprofloxacin or

norfloxacin just as they could to older nonfluorinated quinolones, such as nalidixic acid and oxolinic acid. Fortunately, for many bacterial species the frequency of a mutation conferring resistance to ciprofloxacin or norfloxacin is 100 to 1000 times lower than for nalidixic acid, and the level of resistance attained in a single step is usually lower than the achievable serum quinolone concentration (Ref. 112).

Quinolones antagonize bacteria by inhibiting DNA gyrase, an essential bacterial enzyme with A and B subunits. Some Esch. coli mutants resistant to quinolones have a gyrase target altered in either the A or B subunit at particular sites (Ref. 113,114). In other mutants, the amount of an outer-membrane porin **protein** (OmpF) is diminished and the accumulation of quinolones is decreased. This decreased accumulation is energy-dependent and may require an active quinolone efflux system located on the inner bacterial membrane (Ref. 115,116). Mutants or clinical isolates with the highest levels of fluoroquinolone resistance generally have alterations in both the gyrase target and the accumulation of drugs. Resistance to fluoroquinolone that is mediated by plasmid-encoded genes (Ref. 117) or by drug modification or destruction has not yet been documented.

Mutations in DNA gyrase confer resistance only to quinolones, but alterations in outer-membrane **proteins** provide cross-resistance to chemically unrelated antibiotics such as tetracycline and chloramphenicol (Ref. 112). Conversely, low levels of tetracycline or chloramphenicol can select Esch. coli mutants that also have low-level resistance to fluoroquinolones. From such a multiple-antibiotic-resistant (Mar) mutant, high-level resistance to norfloxacin can be selected at a frequency 1000 times greater than from a nonmutant mar(sup +) cell, thus illustrating how exposure to multiple antibiotics could elicit otherwise rare events (Ref. 118).

Mutants with low-level resistance to multiple antimicrobial agents, including quinolones, have been selected from Ent. **cloacae** , K. pneumoniae, P. aeruginosa, Ser. marcescens, and other gram-negative organisms (Ref. 119). Typical findings are shown in Table 4. Clinical isolates with similar properties have also been described (Ref. 126-128). Despite this potential for resistance, at present most clinical isolates remain susceptible to fluoroquinolones. There are indications, however, that resistance to quinolones is increasing in P. aeruginosa (Ref. 129) and in both coagulase-positive (Ref. 130) and coagulase-negative (Ref. 131) staphylococci. *Table 4. Effects of Alterations in Outer-Membrane **Proteins** on Susceptibility to Antimicrobial Agents *. **TABLE OMITTED**

Evolution of Resistance to Multiple Antibiotics

All too often, resistant clinical isolates are resistant to a number of useful antimicrobial agents. ``Multiresistance'' occurs when the same mechanism confers resistance to several agents, such as those that share a common porin pathway into the cell (Table 4) or have a common target for a particular modifying enzyme (Table 3). There is also a strong tendency for individual resistance genes to cluster, sometimes on the bacterial chromosome, as is the case for methicillin-resistant Staph. aureus, but more often on resistance (R) plasmids. Resistant Enterobacteriaceae frequently contain multiple plasmids, the larger of which can carry genes for resistance to 10 or more antimicrobial agents. In part this is the result of having survived in a nosocomial environment in which multiple antibiotics are employed, but it also reflects how R plasmids evolved.

Plasmids have been found in gram-negative bacteria preserved since the pre-antibiotic era that resemble those now recognized as R plasmids, except that the early isolates lack resistance genes (Ref. 132). Resistance genes on contemporary plasmids are often associated with mobile genetic elements, being either near an insertion sequence or part of a transposon. Both kinds of element facilitate rearrangements of DNA that could result in the acquisition of resistance genes by a plasmid (Ref. 133). In addition, a new type of DNA element has recently been described on a number of plasmids that includes a site-specific integration system that facilitates the capture of resistance genes and also provides a promoter sequence for their efficient expression (Ref. 134-136). The operation of such a unit can result in tandem linkage of resistance genes, such as the all too convenient (from the point of view of the bacterium) association on one plasmid of resistance to both sulfonamides and trimethoprim. Another aspect of multiresistance is that any one of the antimicrobial agents affected can maintain selection for resistance to the group, as is illustrated by the need to restrict the use of kanamycin and tetracycline as well as

ampicillin and carbenicillin to rid a burn unit of P. aeruginosa with plasmids encoding linked resistance to carbenicillin, kanamycin, and tetracycline (Ref. 137).

Staph. aureus is a relatively recent example of the construction and global spread of a multiresistant pathogen. A compilation of the resistance phenotypes and the location of their genes is shown in Table 5 (for a comprehensive review, see Lyon and Skurray (Ref. 106)). Methicillin-resistant Staph. aureus typically carry four or more of the resistance genes shown in Table 5. The accumulation of genes is often associated with one particular insertion sequence-like element (Ref. 141,142) that either provides independent mobility or serves as a fixed site for recombination, allowing individual genes or entire plasmids to change their genetic location. *Table 5. Multiresistance in Staphylococci *. **TABLE OMITTED**

Origin and Dissemination of Resistance Genes

The theory that some resistance genes originated as a protective mechanism for an antibiotic-producing organism has been validated by the finding of aminoglycoside-modifying enzymes in aminoglycoside-producing **strains** of streptomyces (Ref. 143) that have marked homology to modifying enzymes found in bacteria resistant to aminoglycosides (Ref. 144). DNA sequencing has also revealed fundamental similarities between resistance genes found in gram-positive bacteria and those found in gram-negative bacteria, including plasmid-mediated beta-lactamase, (Ref. 145) aminoglycoside-modifying enzymes, (Ref. 146) and genes for tetracycline resistance (Ref. 19). One of the determinants of tetracycline resistance, Tet M, is particularly common, having been identified in gram-positive staphylococci, streptococci, and enterococci; gram-negative Gardnerella vaginalis, H. ducreyi, N. gonorrhoeae, and N. meningitidis; anaerobic Clostridium difficile, Fusobacterium nucleatum, and peptostreptococcus species; and Mycoplasma hominis and Ureaplasma urealyticum (Ref. 147). Carriage of Tet M by a conjugative transposon is a likely explanation for this wide distribution (Ref. 148).

The transposability of TEM beta-lactamase (Ref. 149) has also facilitated its spread to new hosts. The appearance of the TEM enzyme in H. influenzae and N. gonorrhoeae in the 1970s was due to the insertion of all or part of a TEM transposon into previously cryptic plasmids present in these organisms, converting them to beta-lactamase production (Ref. 150). Currently in the United States, 20 percent of H. influenzae isolates (but 32 percent of type b) (Ref. 151and 4.5 percent of gonococcal isolates (but more than 20 percent in some large metropolitan centers) (Ref. 152) produce beta-lactamase. After further delay, TEM-1 beta-lactamase has recently appeared in N. meningitidis (Ref. 153). The ability to produce beta-lactamase is also spreading among gram-positive organisms. Enterococcus faecalis was first found to produce beta-lactamase in 1983, (Ref. 154) and since then enterococcal isolates producing the enzyme have been increasingly recognized (Ref. 155). The beta-lactamase structural gene has been shown to hybridize with a staphylococcal beta-lactamase gene probe, (Ref. 156) but the enzyme is expressed in the streptococcal host at a low, constitutive level instead of being inducible, as in staphylococci. Production of beta-lactamase enhances resistance to ampicillin or penicillin and prevents the bactericidal activity of combinations of aminoglycosides and penicillins. The production of beta-lactamase has not yet been reported in other streptococcal species, but the possibility that the beta-lactamase gene could spread further on a plasmid with a broad range of streptococcal hosts is indeed disquieting.

These examples illustrate that resistance genes are not as confined to particular bacterial species as are the plasmids that so often carry them, but rather have the potential for wide distribution among bacteria. Table 6 summarizes resistance mechanisms for particular organisms. An important corollary of this wide dissemination is that the inappropriate use of antibiotics, whether in humans or in animals, can encourage the selection of resistance and that resistance selected in a harmless bacterium may ultimately cause problems in a pathogenic one. *Table 6. Major Resistance Mechanisms Present in Particular Organisms *. **TABLE OMITTED**

Prospects for the Future

If current practice prevails, the trends in antimicrobial resistance seen in the past decade will continue into the next century. Developing countries and hospitals will be the breeding grounds and reservoirs for the evolution and maintenance of resistance genes and multiresistant **strains**

that will impede both current and future chemotherapy. There are two chief areas of concern. The first is that pathogens for the normal host will acquire a critical complement of resistance and virulence genes, leading to widespread dissemination and serious infection in the community. The second is that bacteria resistant to all available chemotherapy will become the predominant nosocomial pathogens. The specter of draconian isolation precautions and closed wards looms over the latter possibility. What can be done to alter these gloomy prospects? Of foremost importance is the continued effort to control the use of antimicrobial agents in both humans and animals. Guidelines developed under the auspices of the Infectious Diseases Society of America for improving the use of antimicrobial agents by hospitals (Ref. 176) and a comprehensive report by a National Academy of Science and Institute of Medicine panel detailing the risks and benefits of the use of antimicrobial agents in animal feed (Ref. 177) are important efforts to deal with aspects of the problem of the use of antimicrobial agents in this country. Worldwide surveillance for resistance will help identify factors leading to the emergence and spread of resistant isolates in developing countries and may uncover new resistance genes that will alert the world to impending problems (Ref. 2).

Continued efforts by the pharmaceutical industry to develop new antimicrobial agents should be based on knowledge of resistance mechanisms (Ref. 178). Agents targeted to block specific resistance mechanisms, like the beta-lactamase inhibitors clavulanic acid and sulbactam, should be sought. ``Designer drugs'' engineered to thwart specific resistance-gene products and drug modeling to produce agents that inhibit new bacterial targets are increasingly feasible (Ref. 179). Perhaps novel antimicrobial agents directed at hardy nosocomial pathogens should be used initially in combination to limit the emergence of resistance, in the manner of chemotherapy for Mycobacterium tuberculosis (Ref. 180).

Finally, molecular geneticists may be able to engineer genes capable of inactivating specific determinants of resistance. Carried in ``Trojan-horse'' bacteria that are preferential colonizers, these antiresistance genes could be selected for dissemination. Although this scheme may seem futuristic, it is likely to be through the powerful tools of molecular biology and computer modeling that we shall acquire novel weapons with which to wage war against antimicrobial resistance in the 21st century

CITED REFERENCES

1. Holmberg SD, Solomon SL, Blake PA. Health and economic impacts of antimicrobial resistance. Rev Infect Dis 1987; 9:1065-78.
2. Levy SB, Burke JP, Wallace CK, eds. Antibiotic use and antibiotic resistance worldwide. Rev Infect Dis 1987; 9:Suppl 3.
3. Phelps CE. Bug/drug resistance: sometimes less is more. Med Care 1989; 27:194-203.
4. Lester SC, del Pilar Pla M, Wang F, Schael IP, Jiang H, O'Brien TF. The carriage of Escherichia coli resistant to antimicrobial agents by healthy children in Boston, in Caracas, Venezuela, and in Qin Pu, China. N Engl J Med 1990; 323:285-9.
5. Hummel H, Bock A. Ribosomal changes resulting in antimicrobial resistance. In: Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989:193-225.
6. Spratt BG. Resistance to beta-lactam antibiotics mediated by alterations of penicillin-binding **proteins** . In: Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989:77-100.
7. Wolfson JS, Hooper DC. Fluoroquinolone antimicrobial agents. Clin Microbiol Rev 1989; 2:378-424.
8. Ezekiel DH, Hutchins JE. Mutations affecting RNA polymerase associated with rifampicin resistance in Escherichia coli. Nature 1968; 220:276-7.
9. Wise EM Jr, Abou-Donia MM. Sulfonamide resistance mechanism in Escherichia coli: R plasmids can determine sulfonamide-resistant dihydropteroate synthases. Proc Natl Acad Sci U S A 1975; 72:2621-5.
10. Manavathu EK, Fernandez CL, Cooperman BS, Taylor DE. Molecular studies on the mechanism of tetracycline resistance mediated by Tet(O). Antimicrob Agents Chemother 1990; 34:71-7.
11. Huovinen P. Trimethoprim resistance. Antimicrob Agents Chemother 1987;

31:1451-6.
12. al-Obeid S, Collatz E, Gutmann L. Mechanism of resistance to vancomycin in Enterococcus faecium D366 and Enterococcus faecalis A256. Antimicrob Agents Chemother 1990; 34:252-6.
13. Davies JE. Aminoglycoside-aminocyclitol antibiotics and their modifying enzymes. In: Lorian V, ed. Antibiotics in laboratory medicine. 2nd ed. Baltimore: Williams & Wilkins, 1986:790-809.
14. Medeiros AA. Plasmid-determined beta-lactamases. In: Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989:101-27.
15. Sanders CC. The chromosomal beta-lactamases. In: Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989:129-49.
16. Shaw WV. Chloramphenicol acetyltransferase: enzymology and molecular biology. CRC Crit Rev Biochem 1983; 14:1-46.
17. Nikaido H. Role of the outer membrane of Gram-negative bacteria in antimicrobial resistance. In: Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989:1-34.
18. Goldman RC, Capobianco JO. Role of an energy-dependent efflux pump in plasmid pNE24-mediated resistance to 14- and 15-membered macrolides in Staphylococcus epidermidis. Antimicrob Agents Chemother 1990; 34:1973-80.
19. Levy SB. Evolution and spread of tetracycline resistance determinants. J Antimicrob Chemother 1989; 24:1-3.
20. Levy SB. Resistance to the tetracyclines. In: Bryan LE, ed. Antimicrobial drug resistance. Orlando, Fla.: Academic Press, 1984:191-240.
21. Jacoby GA, Swartz MN. Plasmids: microbiologic and clinical importance. Semin Infect Dis 1980; 3:1-37.
22. Finland M. Emergence of antibiotic-resistant bacteria. N Engl J Med 1955; 253:909-22, 969-79, 1019-28.
23. Davies J, Smith DI. Plasmid-determined resistance to antimicrobial agents. Annu Rev Microbiol 1978; 32:469-518.
24. Foster TJ. Plasmid-determined resistance to antimicrobial drugs and toxic metal ions in bacteria. Microbiol Rev 1983; 47:361-409.
25. Bryan LE, ed. Microbial resistance to drugs. Vol. 91 of Handbook of experimental pharmacology. Berlin, Germany: Springer-Verlag, 1989.
26. Korfmann G, Wiedemann B. Genetic control of beta-lactamase production in Enterobacter **cloacae** . Rev Infect Dis 1988; 10:793-9.
27. Then RL, Angehrn P. Trapping of nonhydrolyzable cephalosporins by cephalosporinases in Enterobacter **cloacae** and Pseudomonas aeruginosa as a possible resistance mechanism. Antimicrob Agents Chemother 1982; 21:711-7.
28. Vu H, Nikaido H. Role of beta-lactam hydrolysis in the mechanism of resistance of a beta-lactamase-constitutive Enterobacter **cloacae strain** to expanded-spectrum beta-lactams. Antimicrob Agents Chemother 1985; 27:393-8.
29. Sanders WE Jr, Sanders CC. Inducible beta-lactamases: clinical and epidemiologic implications for use of newer cephalosporins. Rev Infect Dis 1988; 10:830-8.
30. Olsson O, Bergstrom S, Lindberg FP, Normark S. ampC beta-lactamase hyperproduction in Escherichia coli: natural ampicillin resistance generated by horizontal chromosomal DNA transfer from Shigella. Proc Natl Acad Sci U S A 1983; 80:7556-60.
31. Knothe H, Shah P, Krcmery V, Antal M, Mitsuhashi S. Transferable resistance to cefotaxime, cefoxitin, cefamandole and cefuroxime in clinical isolates of Klebsiella pneumoniae and Serratia marcescens. Infection 1983; 11:315-7.
32. Kliebe C, Nies BA, Meyer JF, Tolxdorff-Neutzling RM, Wiedemann B. Evolution of plasmid-coded resistance to broad-spectrum cephalosporins. Antimicrob Agents Chemother 1985; 28:302-7.
33. Philippon A, Labia R, Jacoby G. Extended-spectrum beta-lactamases. Antimicrob Agents Chemother 1989; 33:1131-6.
34. Philippon A, Ben Redjeb S, Fournier G, Ben Hassen A. Epidemiology of extended spectrum beta-lactamases. Infection 1989; 17:347-54.
35. Jacoby GA, Carreras I. Activities of beta-lactam antibiotics against Escherichia coli **strains** producing extended-spectrum beta-lactamases. Antimicrob Agents Chemother 1990; 34:858-62.

36. Mabilat C, Courvalin P. Development of ``oligotyping'' for characterization and molecular epidemiology of TEM beta-lactamases in members of the family Enterobacteriaceae. Antimicrob Agents Chemother 1990; 34:2210-6.
37. Gutmann L, Kitzis MD, Billot-Klein D, et al Plasmid-mediated beta-lactamase (TEM-7) involved in resistance to ceftazidime and aztreonam. Rev Infect Dis 1988; 10:860-6.
38. Sougakoff W, Goussard S, Gerbaud G, Courvalin P. Plasmid-mediated resistance to third-generation cephalosporins caused by point mutations in TEM-type penicillinase genes. Rev Infect Dis 1988; 10:879-84.
39. Papanicolaou GA, Medeiros AA, Jacoby GA. Novel plasmid-mediated beta-lactamase (MIR-1) conferring resistance to oxyimino- and alpha-methoxy beta-lactams in clinical isolates of Klebsiella pneumoniae. Antimicrob Agents Chemother 1990; 34:2200-9.
40. Yang Y, Wu P, Livermore DM. Biochemical characterization of a beta-lactamase that hydrolyzes penems and carbapenems from two Serratia marcescens isolates. Antimicrob Agents Chemother 1990; 34:755-8.
41. Cuchural GJ Jr, Malamy MH, Tally FP. beta-Lactamase-mediated imipenem resistance in Bacteroides fragilis. Antimicrob Agents Chemother 1986; 30:645-8.
42. Dufresne J, Vezina G, Levesque RC. Cloning and expression of the imipenem-hydrolyzing beta-lactamase operon from Pseudomonas maltophilia in Escherichia coli. Antimicrob Agents Chemother 1988; 32:819-26.
43. Bellido F, Veuthey C, Blaser J, Bauernfeind A, Pechere JC. Novel resistance to imipenem associated with an altered PBP-4 in a Pseudomonas aeruginosa clinical isolate. J Antimicrob Chemother 1990; 25:57-68.
44. Pierre J, Boisivon A, Gutmann L. Alteration of PBP 3 entails resistance to imipenem in Listeria monocytogenes. Antimicrob Agents Chemother 1990; 34:1695-8.
45. Trias J, Nikaido H. Outer membrane **protein** D2 catalyzes facilitated diffusion of carbapenems and penems through the outer membrane of Pseudomonas aeruginosa. Antimicrob Agents Chemother 1990; 34:52-7.
46. Hopkins JM, Towner KJ. Enhanced resistance to cefotaxime and imipenem associated with outer membrane **protein** alterations in Enterobacter aerogenes. J Antimicrob Chemother 1990; 25:49-55.
47. Kernodle DS, Stratton CW, McMurray LW, Chipley JR, McGraw PA. Differentiation of beta-lactamase variants of Staphylococcus aureus by substrate hydrolysis profiles. J Infect Dis 1989; 159:103-8.
48. Kernodle DS, Classen DC, Burke JP, Kaiser AB. Failure of cephalosporins to prevent Staphylococcus aureus surgical wound infections. JAMA 1990; 263:961-6.
49. McDougal LK, Thornsberry C. The role of beta-lactamase in staphylococcal resistance to penicillinase-resistant penicillins and cephalosporins. J Clin Microbiol 1986; 23:832-9.
50. Chambers HF, Archer G, Matsuhashi M. Low-level methicillin resistance in **strains** of Staphylococcus aureus. Antimicrob Agents Chemother 1989; 33:424-8.
51. Massanari RM, Pfaller MA,Wakefield DS, et al Implications of acquired oxacillin resistance in the management and control of Staphylococcus aureus infections. J Infect Dis 1988; 158:702-9.
52. Pierre J, Williamson R, Bornet M, Gutmann L. Presence of an additional penicillin-binding **protein** in methicillin-resistant Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, and Staphylococcus simulans with a low affinity for methicillin, cephalothin, and cefamandole. Antimicrob Agents Chemother 1990; 34:1691-4.
53. Tomasz A, Drugeon HB, de Lencastre HM, Jabes D, McDougall L, Bille J. New mechanism for methicillin resistance in Staphylococcus aureus: clinical isolates that lack the PBP 2a gene and contain normal penicillin-binding **proteins** with modified penicillin-binding capacity. Antimicrob Agents Chemother 1989; 33:1869-74.
54. Brumfitt W, Hamilton-Miller J. Methicillin-resistant Staphylococcus aureus. N Engl J Med 1989; 320:1188-96.
55. Maple PAC, Hamilton-Miller JMT, Brumfitt W. World-wide antibiotic resistance in methicillin-resistant Staphylococcus aureus. Lancet 1989; 1:537-40.
56. Horan TC, White JW, Jarvis WR, et al Nosocomial infection surveillance, 1984. MMWR CDC Surveill Summ 1986; 35:17SS-29SS.

57. Hsu CC, Macaluso CP, Special L, Hubble RH. High rate of methicillin resistance of Staphylococcus aureus isolated from hospitalized nursing home patients. Arch Intern Med 1988; 148:569-70.
58. Jones RN, Barry AL, Gardiner RV, Packer RR. The prevalence of staphylococcal resistance to penicillinase-resistant penicillins: a retrospective and prospective national surveillance trial of isolates from 40 medical centers. Diagn Microbiol Infect Dis 1989; 12:385-94.
59. Froggatt JW, Johnston JL, Galetto DW, Archer GL. Antimicrobial resistance in nosocomial isolates of Staphylococcus haemolyticus. Antimicrob Agents Chemother 1989; 33:460-6.
60. Ubukata K, Nonoguchi R, Matsuhashi M, Konno M. Expression and inducibility in Staphylococcus aureus of the mecA gene, which encodes a methicillin-resistant S. aureus-specific penicillin-binding **protein** . J Bacteriol 1989; 171:2882-5.
61. Song MD, Wachi M, Doi M, Ishino F, Matsuhashi M. Evolution of an inducible penicillin-target **protein** and methicillin-resistant Staphylococcus aureus by gene fusion. FEBS Lett 1987; 221:167-71.
62. Chambers HF, Hackbarth CJ. Effect of NaCl and nafcillin on penicillin-binding **protein** 2a and heterogeneous expression of methicillin resistance in Staphylococcus aureus. Antimicrob Agents Chemother 1987; 31:1982-8.
63. Berger-Bachi B, Barberis-Maino L, Strassle A, Kayser FH. FemA, a host-mediated factor essential for methicillin resistance in Staphylococcus aureus: molecular cloning and characterization. Mol Gen Genet 1989; 219:263-9.
64. Berger-Bachi B, Kohler M. A novel site on the chromosome of Staphylococcus aureus influencing the level of methicillin resistance: genetic mapping. FEMS Microbiol Lett 1983; 20:305-9.
65. Tesch W, Ryffel C, Strassle A, Kayser FH, Berger-Bachi B. Evidence of a novel staphylococcal mec-encoded element (mecR) controlling expression of penicillin-binding **protein** 2'. Antimicrob Agents Chemother 1990; 34:1703-6.
66. Chambers HF. Methicillin-resistant staphylococci. Clin Microbiol Rev 1988; 1:173-86.
67. Archer GL, Pennell E. Detection of methicillin resistance in staphylococci by using a DNA probe. Antimicrob Agents Chemother 1990; 34:1720-4.
68. Fontana R, Canepari P, Lleo MM, Satta G. Mechanisms of resistance of enterococci to beta-lactam antibiotics. Eur J Clin Microbiol Infect Dis 1990; 9:103-5.
69. Jabes D, Nachman S, Tomasz A. Penicillin-binding **protein** families: evidence for the clonal nature of penicillin resistance in clinical isolates of pneumococci. J Infect Dis 1989; 159:16-25.
70. Dowson CG, Hutchison A, Brannigan JA, et al Horizontal transfer of penicillin-binding **protein** genes in penicillin-resistant clinical isolates of Streptococcus pneumoniae. Proc Natl Acad Sci U S A 1989; 86:8842-6.
71. Simberkoff MS, Lukaszewki M, Cross A, et al Antibiotic-resistant isolates of Streptococcus pneumoniae from clinical specimens: a cluster of serotype 19A organisms in Brooklyn, New York. J Infect Dis 1986; 153:78-82.
72. Viladrich PF, Gudiol F, Linares J, Rufi G, Ariza J, Pallares R. Characteristics and antibiotic therapy of adult meningitis due to penicillin-resistant pneumococci. Am J Med 1988; 84:839-46.
73. Pallares R, Gudiol F, Linares J, et al Risk factors and response to antibiotic therapy in adults with bacteremic pneumonia caused by penicillin-resistant pneumococci. N Engl J Med 1987; 317:18-22.
74. Facklam R, Carey R. Streptococci and aerococci. In: Lennette EH, Balows A, Hausler WJ Jr, Shadomy HJ, eds. Manual of clinical microbiology. 4th ed. Washington, D.C.: American Society for Microbiology, 1985:154-75.
75. Mendelman PM, Chaffin DO, Kalaitzoglou G. Penicillin-binding **proteins** and ampicillin resistance in Haemophilus influenzae. J Antimicrob Chemother 1990; 25:525-34.
76. Dougherty TJ. Genetic analysis and penicillin-binding **protein** alterations in Neisseria gonorrhoeae with chromosomally mediated resistance. Antimicrob Agents Chemother 1986; 30:649-52.
77. Mendelman PM, Campos J, Chaffin DO, Serfass DA, Smith AL, Saez-Nieto JA. Relative penicillin G resistance in Neisseria meningitidis and reduced affinity of penicillin-binding **protein** 3. Antimicrob Agents

Chemother 1988; 32:706-9.
78. Spratt BG, Zhang Q-Y, Jones DM, Hutchison A, Brannigan JA, Dowson CG. Recruitment of a penicillin-binding **protein** gene from Neisseria flavescens during the emergence of penicillin resistance in Neisseria meningitidis. Proc Natl Acad Sci U S A 1989; 86:8988-92.
79. Spratt BG. Hybrid penicillin-binding **proteins** in penicillin-resistant **strains** of Neisseria gonorrhoeae. Nature 1988; 332:173-6.
80. Handwerger S, Horowitz H, Coburn K, Kolokathis A, Wormser GP. Infection due to Leuconostoc species: six cases and review. Rev Infect Dis 1990; 12:602-10.
81. Ruoff KL, Kuritzkes DR, Wolfson JS, Ferraro MJ. Vancomycin-resistant gram-positive bacteria isolated from human sources. J Clin Microbiol 1988; 26:2064-8.
82. Schwalbe RS, Stapleton JT, Gilligan PH. Emergence of vancomycin resistance in coagulase-negative staphylococci. N Engl J Med 1987; 316:927-31.
83. Leclerq R, Derlot E, Duval J, Courvalin P. Plasmid-mediated resistance to vancomycin and teicoplanin in Enterococcus faecium. N Engl J Med 1988; 319:157-61.
84. Shlaes DM, Bouvet A, Devine C, Shlaes JH, al-Obeid S, Williamson R. Inducible, transferable resistance to vancomycin in Enterococcus faecalis A256. Antimicrob Agents Chemother 1989; 33:198-203.
85. Reynolds PE. Structure, biochemistry and mechanism of action of glycopeptide antibiotics. Eur J Clin Microbiol Infect Dis 1990; 8:943-50.
86. Uttley AH, Collins CH, Naidoo J, George RC. Vancomycin-resistant enterococci. Lancet 1988; 1:57-8.
87. Sahm DF, Kissinger J, Gilmore MS, et al In vitro susceptibility studies of vancomycin-resistant Enterococcus faecalis. Antimicrob Agents Chemother 1989; 33:1588-91.
88. Gerding DN, Larson TA. Aminoglycoside resistance in gram-negative bacilli during increased amikacin use. Am J Med 1985; 79:Suppl 1A:1-7.
89. Vanhoof R, Hubrechts JM, Nyssen HJ, Roebben E. Three-year survey of amikacin use and aminoglycoside resistance in a general hospital in Belgium. Eur J Clin Microbiol Infect Dis 1988; 7:183-5.
90. Young EJ, Sewell MC, Koza MA, Clarridge JE. Antibiotic resistance patterns during aminoglycoside restriction. Am J Med Sci 1985; 290:223-7.
91. Levine JF, Maslow MJ, Leibowitz RE, et al Amikacin-resistant gram-negative bacilli: correlation of occurrence with amikacin use. J Infect Dis 1985; 151:295-300.
92. Gaynes R, Groisman E, Nelson E, Casadaban M, Lerner SA. Isolation, characterization, and cloning of a plasmid-borne gene encoding a phosphotransferase that confers high-level amikacin resistance in enteric bacilli. Antimicrob Agents Chemother 1988; 32:1379-84.
93. Jacoby GA, Blaser MJ, Santanam P, et al Appearance of amikacin and tobramycin resistance due to 4'-aminoglycoside nucleotidyltransferase ANT(4')-II] in gram-negative pathogens. Antimicrob Agents Chemother 1990; 34:2381-6.
94. Maloney J, Rimland D, Stephens DS, Terry P, Whitney AM. Analysis of amikacin-resistant Pseudomonas aeruginosa developing in patients receiving amikacin. Arch Intern Med 1989; 149:630-4.
95. Lambert T, Gerbaud G, Courvalin P. Transferable amikacin resistance in Acinetobacter spp. due to a new type of 3'-aminoglycoside phosphotransferase. Antimicrob Agents Chemother 1988; 32:15-9.
96. Lambert T, Gerbaud G, Bouvet P, Vieu J-F, Courvalin P. Dissemination of amikacin resistance gene aphA6 in Acinetobacter spp. Antimicrob Agents Chemother 1990; 34:1244-8.
97. Kettner M, Macickova T, Navarova J, Krcmery V, Havlik J. Mechanisms of transferable amikacin resistance in enterobacteria in a Czechoslovak clinic. J Antimicrob Chemother 1988; 22:82-4.
98. Shimizu K, Kumada T, Hsieh W-C, et al Comparison of aminoglycoside resistance patterns in Japan, Formosa, and Korea, Chile, and the United States. Antimicrob Agents Chemother 1985; 28:282-8.
99. Ubukata K, Yamashita N, Gotoh A, Konno M. Purification and characterization of aminoglycoside-modifying enzymes from Staphylococcus aureus and Staphylococcus epidermidis. Antimicrob Agents Chemother 1984; 25:754-9.
100. Kettner M, Macickova T, Krcmery V. Occurrence of

4'-O-aminoglycoside-nucleotidyltransferase in clinical **strains** of Enterobacteriaceae. Infection 1989; 17:100-1.
101. Thorbjarnardottir SH, Magnusdottir RA, Eggertsson G. Mutations determining generalized resistance to aminoglycoside antibiotics in Escherichia coli. Mol Gen Genet 1978; 161:89-98.
102. Bryan LE, O'Hara K, Wong S. Lipopolysaccharide changes in impermeability-type aminoglycoside resistance in Pseudomonas aeruginosa. Antimicrob Agents Chemother 1984; 26:250-5.
103. Tran Van Nhieu G, Collatz E. Heterogeneity of 6'-N-acetyltransferases of type 4 conferring resistance to amikacin and related aminoglycosides in members of the family Enterobacteriaceae. Antimicrob Agents Chemother 1988; 32:1289-91.
104. Ferretti JJ, Gilmore KS, Courvalin P. Nucleotide sequence analysis of the gene specifying the bifunctional 6'-aminoglycoside acetyltransferase 2''-aminoglycoside phosphotransferase enzyme in Streptococcus faecalis and identification and cloning of gene regions specifying the two activities. J Bacteriol 1986; 167:631-8.
105. Thomas WD Jr, Archer GL. Mobility of gentamicin resistance genes from staphylococci isolated in the United States: identification of Tn4031, a gentamicin resistance transposon from Staphylococcus epidermidis. Antimicrob Agents Chemother 1989; 33:1335-41.
106. Lyon BR, Skurray R. Antimicrobial resistance of Staphylococcus aureus: genetic basis. Microbiol Rev 1987; 51:88-134.
107. Forbes BA, Schaberg DR. Transfer of resistance plasmids from Staphylococcus epidermidis to Staphylococcus aureus: evidence for conjugative exchange of resistance. J Bacteriol 1983; 153:627-34.
108. Archer GL, Dietrick DR, Johnston JL. Molecular epidemiology of transmissible gentamicin resistance among coagulase-negative staphylococci in a cardiac surgery unit. J Infect Dis 1985; 151:243-51.
109. Ounissi H, Derlot E, Carlier C, Courvalin P. Gene homogeneity for aminoglycoside-modifying enzymes in gram-positive cocci. Antimicrob Agents Chemother 1990; 34:2164-8.
110. Patterson JE, Zervos MJ. High-level gentamicin resistance in Enterococcus: microbiology, genetic basis, and epidemiology. Rev Infect Dis 1990; 12:644-52.
111. Hodel-Christian SL, Murray BE. Mobilization of the gentamicin resistance gene in Enterococcus faecalis. Antimicrob Agents Chemother 1990; 34:1278-80.
112. Hooper DC, Wolfson JS, Souza KS, Tung C, McHugh GL, Swartz MN. Genetic and biochemical characterization of norfloxacin resistance in Escherichia coli. Antimicrob Agents Chemother 1986; 29:639-44.
113. Nakamura S, Nakamura M, Kojima T, Yoshida H. gyrA and gyrB mutations in quinolone-resistant **strains** of Escherichia coli. Antimicrob Agents Chemother 1989; 33:254-5.
114. Yoshida H, Bogaki M, Nakamura M, Nakamura S. Quinolone resistance-determining region in the DNA gyrase gyrA gene of Escherichia coli. Antimicrob Agents Chemother 1990; 34:1271-2.
115. Hooper DC, Wolfson JS, Souza KS, Ng EY, McHugh GL, Swartz MN. Mechanisms of quinolone resistance in Escherichia coli: characterization of nfxB and cfxB, two mutant resistance loci decreasing norfloxacin accumulation. Antimicrob Agents Chemother 1989; 33:283-90.
116. Cohen S, Hooper DC, Wolfson JS, Souza KS, McMurry LM, Levy SB. Endogenous active efflux of norfloxacin in susceptible Escherichia coli. Antimicrob Agents Chemother 1988; 32:1187-91.
117. Courvalin P. Plasmid-mediated 4-quinolone resistance: a real or apparent absence? Antimicrob Agents Chemother 1990; 34:681-4.
118. Cohen SP, McMurry LM, Hooper DC, Wolfson JS, Levy SB. Cross-resistance to fluoroquinolones in multiple-antibiotic resistant (Mar) Escherichia coli selected by tetracycline or chloramphenicol: decreased drug accumulation associated with membrane changes in addition to OmpF reduction. Antimicrob Agents Chemother 1989; 33:1318-25.
119. Sanders CC, Sanders WE Jr, Goering RV, Werner V. Selection of multiple antibiotic resistance by quinolones, beta-lactams, and aminoglycosides with special reference to cross-resistance between unrelated drug classes. Antimicrob Agents Chemother 1984; 26:797-801.
120. Harder KJ, Nikaido H, Matsuhashi M. Mutants of Escherichia coli that are resistant to certain beta-lactam compounds lack the ompF porin.

Antimicrob Agents Chemother 1981; 20:549-52.
121. Jaffe A, Chabbert YA, Derlot E. Selection and characterization of beta-lactam-resistant Escherichia coli K-12 mutants. Antimicrob Agents Chemother 1983; 23:622-5.
122. George AM, Levy SB. Amplifiable resistance to tetracycline, chloramphenicol, and other antibiotics in Escherichia coli: involvement of a non-plasmid-determined efflux of tetracycline. J Bacteriol 1983; 155:531-40.
123. Robillard NJ, Scarpa AL. Genetic and physiological characterization of ciprofloxacin resistance in Pseudomonas aeruginosa PAO. Antimicrob Agents Chemother 1988; 32:535-9.
124. Chamberland S, Bayer AS, Schollaardt T, Wong SA, Bryan LE. Characterization of mechanisms of quinolone resistance in Pseudomonas aeruginosa **strains** isolated in vitro and in vivo during experimental endocarditis. Antimicrob Agents Chemother 1989; 33:624-34.
125. Gutmann L, Williamson R, Moreau N, et al Cross-resistance to nalidixic acid, trimethoprim, and chloramphenicol associated with alterations in outer membrane **proteins** of Klebsiella, Enterobacter, and Serratia. J Infect Dis 1985; 151:501-7.
126. Aoyama H, Fujimaki K, Sato K, et al Clinical isolate of Citrobacter freundii highly resistant to new quinolones. Antimicrob Agents Chemother 1988; 32:922-4.
127. Sanders CC, Watanakunakorn C. Emergence of resistance to beta-lactams, aminoglycosides, and quinolones during combination therapy for infection due to Serratia marcescens. J Infect Dis 1986; 153:617-9.
128. Daikos GL, Lolans VT, Jackson GG. Alterations in outer membrane **proteins** of Pseudomonas aeruginosa associated with selective resistance to quinolones. Antimicrob Agents Chemother 1988; 32:785-7.
129. Kresken M, Wiedemann B. Development of resistance to nalidixic acid and the fluoroquinolones after the introduction of norfloxacin and ofloxacin. Antimicrob Agents Chemother 1988; 32:1285-8.
130. Schaefler S. Methicillin-resistant **strains** of Staphylococcus aureus resistant to quinolones. J Clin Microbiol 1989; 27:335-6.
131. Kotilainen P, Nikoskelainen J, Huovinen P. Emergence of ciprofloxacin-resistant coagulase-negative staphylococcal skin flora in immunocompromised patients receiving ciprofloxacin. J Infect Dis 1990; 161:41-4.
132. Datta N, Hughes VM. Plasmids of the same Inc groups in Enterobacteria before and after the medical use of antibiotics. Nature 1983; 306:616-7.
133. Kleckner N. Transposable elements in prokaryotes. Annu Rev Genet 1981; 15:341-404.
134. Stokes HW, Hall RM. A novel family of potentially mobile DNA elements encoding site-specific gene-integration functions: integrons. Mol Microbiol 1989; 3:1669-83.
135. Martinez E, de la Cruz F. Genetic elements involved in Tn21 site-specific integration, a novel mechanism for the dissemination of antibiotic resistance genes. EMBO J 1990; 9:1275-81.
136. Mercier J, Lachapelle J, Couture F, et al Structural and functional characterization of tnpI, a recombinase locus in Tn21 and related beta-lactamase transposons. J Bacteriol 1990; 172:3745-57.
137. Lowbury EJL, Babb JR, Roe E. Clearance from a hospital of gram-negative bacilli that transfer carbenicillin-resistance to Pseudomonas aeruginosa. Lancet 1972; 2:941-5.
138. Cookson BD. Mupirocin resistance in staphylococci. J Antimicrob Chemother 1990; 25:497-503.
139. Sreedharan S, Oram M, Jensen B, Peterson LR, Fisher LM. DNA gyrase gyrA mutations in ciprofloxacin-resistant **strains** of Staphylococcus aureus: close similarity with quinolone resistance mutations in Escherichia coli. J Bacteriol 1990; 172:7260-2.
140. Yoshida H, Bogaki M, Nakamura S, Ubukata K, Konno M. Nucleotide sequence and characterization of the Staphylococcus aureus norA gene, which confers resistance to quinolones. J Bacteriol 1990; 172:6942-9.
141. Barberis-Maino L, Berger-Bachi B, Weber H, Beck WD, Kayser FH. IS431, a staphylococcal insertion sequence-like element related to IS26 from Proteus vulgaris. Gene 1987; 59:107-13.
142. Gillespie MT, Lyon BR, Loo LSL, Matthews PR, Stewart PR, Skurray RA. Homologous direct repeat sequences associated with mercury, methicillin, tetracycline and trimethoprim resistance determinants in

Staphylococcus aureus. FEMS Microbiol Lett 1987; 43:165-71.
143. Benveniste R, Davies J. Aminoglycoside antibiotic-inactivating enzymes in actinomycetes similar to those present in clinical isolates of antibiotic-resistant bacteria. Proc Natl Acad Sci U S A 1973; 70:2276-80.
144. Thompson CJ, Gray GS. Nucleotide sequence of a streptomycete aminoglycoside phosphotransferase gene and its relation to phosphotransferases encoded by resistance plasmids. Proc Natl Acad Sci U S A 1983; 80:5190-4.
145. Ambler RP. The structure of beta-lactamases. Philos Trans R Soc Lond Biol] 1980; 289:321-31.
146. Trieu-Cuot P, Courvalin P. Evolution and transfer of aminoglycoside resistance genes under natural conditions. J Antimicrob Chemother 1986; 18:Suppl C:93-102.
147. Roberts MC. Characterization of the Tet M determinants in urogenital and respiratory bacteria. Antimicrob Agents Chemother 1990; 34:476-8.
148. Roberts MC, Kenny GE. Conjugal transfer of transposon Tn916 from Streptococcus faecalis to Mycoplasma hominis. J Bacteriol 1987; 169:3836-9.
149. Hedges RW, Jacob AE. Transposition of ampicillin resistance from RP4 to other replicons. Mol Gen Genet 1974; 132:31-40.
150. Brunton J, Meier M, Erhman N, Clare D, Almawy R. Origin of small beta-lactamase-specifying plasmids in Haemophilus species and Neisseria gonorrhoeae. J Bacteriol 1986; 168:374-9.
151. Doern GV, Jorgensen JH, Thornsberry C, et al National collaborative study of the prevalence of antimicrobial resistance among clinical isolates of Haemophilus influenzae. Antimicrob Agents Chemother 1988; 32:180-5.
152. Moran JS, Zenilman JM. Therapy for gonococcal infections: options in 1989. Rev Infect Dis 1990; 12:S633-S644.
153. Fontanals D, Pineda V, Pons I, Rojo JC. Penicillin-resistant beta-lactamase producing Neisseria meningitidis in Spain. Eur J Clin Microbiol Infect Dis 1989; 8:90-1.
154. Murray BE, Mederski-Samoraj BD. Transferable beta-lactamase: a new mechanism for in vitro penicillin resistance in Streptococcus faecalis. J Clin Invest 1983; 72:1168-71.
155. Patterson JE, Wanger A, Zscheck KK, Zervos MJ, Murray BE. Molecular epidemiology of beta-lactamase-producing enterococci. Antimicrob Agents Chemother 1990; 34:302-5.
156. Murray BE, Mederski-Samoraj B, Foster SK, Brunton JL, Harford P. In vitro studies of plasmid-mediated penicillinase from Streptococcus faecalis suggest a staphylococcal origin. J Clin Invest 1986; 77:289-93.
157. Joly-Guillou ML, Bergogne-Berezin E, Moreau N. Enzymatic resistance to beta-lactams and aminoglycosides in Acinetobacter calcoaceticus. J Antimicrob Chemother 1987; 20:773-6.
158. Wexler HM, Finegold SM. Antimicrobial resistance in Bacteroides. J Antimicrob Chemother 1987; 19:143-6.
159. Park BH, Hendricks M, Malamy MH, Tally FP, Levy SB. Cryptic tetracycline resistance determinant (class F) from Bacteroides fragilis mediates resistance in Escherichia coli by actively reducing tetracycline accumulation. Antimicrob Agents Chemother 1987; 31:1739-43.
160. Breuil J, Dublanchet A, Truffaut N, Sebald M. Transferable 5-nitroimidazole resistance in the Bacteroides fragilis group. Plasmid 1989; 21:151-4.
161. Taylor DE, Courvalin P. Mechanisms of antibiotic resistance in Campylobacter species. Antimicrob Agents Chemother 1988; 32:1107-12.
162. Rood JI, Jefferson S, Bannam TL, Wilkie JM, Mullany P, Wren BW. Hybridization analysis of three chloramphenicol resistance determinants from Clostridium perfringens and Clostridium difficile. Antimicrob Agents Chemother 1989; 33:1569-74.
163. Murray BE. The life and times of the Enterococcus. Clin Microbiol Rev 1990; 3:46-65.
164. Dangor Y, Ballard RC, Miller SD, Koornhof HJ. Antimicrobial susceptibility of Haemophilus ducreyi. Antimicrob Agents Chemother 1990; 34:1303-7.
165. Needham CA. Haemophilus influenzae: antibiotic susceptibility. Clin Microbiol Rev 1988; 1:218-27.

166. Wallace RJ Jr, Nash DR, Steingrube VA. Antibiotic susceptibilities and drug resistance in Moraxella (Branhamella) catarrhalis. Am J Med 1990; 88:Suppl 5A:46S-50S.
167. Sareen M, Khuller GK. Cell wall and membrane changes associated with ethambutol resistance in Mycobacterium tuberculosis H(sub 37)Ra. Antimicrob Agents Chemother 1990; 34:1773-6.
168. Schwarcz SK, Zenilman JM, Schnell D, et al National surveillance of antimicrobial resistance in Neisseria gonorrhoeae. JAMA 1990; 264:1413-7.
169. Morse SA, Johnson SR, Biddle JW, Roberts MC. High-level tetracycline resistance in Neisseria gonorrhoeae is result of acquisition of streptococcal tetM determinant. Antimicrob Agents Chemother 1986; 30:664-70.
170. Kristiansen B-E, Radstrom P, Jenkins A, Ask E, Facinelli B, Skold O. Cloning and characterization of a DNA fragment that confers sulfonamide resistance in a serogroup B, serotype 15 **strain** of Neisseria meningitidis. Antimicrob Agents Chemother 1990; 34:2277-9.
171. Jacoby GA. Resistance plasmids of Pseudomonas. In: Sokatch JR, ed. The biology of Pseudomonas. Vol. 10 of The bacteria: a treatise on structure and function. Orlando, Fla.: Academic Press, 1986:265-93.
172. Prince A, Wood MS, Cacalano GS, Chin NX. Isolation and characterization of a penicillinase from Pseudomonas cepacia 249. Antimicrob Agents Chemother 1988; 32:838-43.
173. Klugman KP. Pneumococcal resistance to antibiotics. Clin Microbiol Rev 1990; 3:171-96.
174. Clewell DB. Plasmids, drug resistance, and gene transfer in the genus Streptococcus. Microbiol Rev 1981; 45:409-36.
175. Horodniceanu T, Buu-Hoi A, Delbos F, Bieth G. High-level aminoglycoside resistance in group A, B, G, D (Streptococcus bovis) and viridans streptococci. Antimicrob Agents Chemother 1982; 21:176-9.
176. Marr JJ, Moffet HL, Kunin CM. Guidelines for improving the use of antimicrobial agents in hospitals: a statement by the Infectious Diseases Society of America. J Infect Dis 1988; 157:869-76.
177. Committee on Human Health Risk Assessment of Using Subtherapeutic Antibiotics in Animal Feed. Human health risks with the subtherapeutic use of penicillin or tetracycline in animal feed. Washington, D.C.: National Academy Press, 1989.
178. Gootz TD. Discovery and development of new antimicrobial agents. Clin Microbiol Rev 1990; 3:13-31.
179. Silver L, Bostian K. Screening of natural products for antimicrobial agents. Eur J Clin Microbiol Infect Dis 1990; 9:455-61.
180. Eliopoulos GM, Eliopoulis CT. Antibiotic combinations: should they be tested? Clin Microbiol Rev 1988; 1:139-56. □

for this discrepancy concerns the cellular ATP levels. In aerobic cells the ATP levels dropped 10- to 15-fold within 1 min of adding KCN and then increased gradually over the next 30 min. Similarly, the addition of 2 mM iodoacetic acid, an inhibitor of glycolysis, to anaerobic, log phase, SDS-containing **cultures** caused rapid lysis. However, unlike the situation for KCN-treated aerobic cells, lysis still occurred when SDS (0.5%) was added 30 min after addition of iodoacetic acid. The reason for this difference is that in anaerobic cells, ATP levels dropped 10- to 12-fold within 5 min of the addition of iodoacetic acid and then did not increase over the next 30 min. Evidence that the energy requirement was for ATP was provided by uptake experiments with [14C]benzoic acid and alpha-[14C] isoaminobutyric acid that showed that the proton gradient (delta pH) and the membrane potential (delta psi) were the same in cells **grown** in the presence or absence of SDS.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Adenosine Triphosphate--metabolism--ME; *Enterobacter cloacae--drug effects--DE; *Sodium Dodecyl Sulfate--pharmacology--PD; Aerobiosis; Drug Resistance; **Enterobacter cloacae** -- **growth** and development--GD; Enterobacter cloacae--metabolism--ME; Glucose--physiology --PH; Hydrogen-Ion Concentration; Iodoacetates--pharmacology--PD; Iodoacetic Acid; Membrane Potentials; Potassium Cyanide--pharmacology--PD

CAS Registry No.: 0 (Iodoacetates); 151-21-3 (Sodium Dodecyl Sulfate) ; 151-50-8 (Potassium Cyanide); 50-99-7 (Glucose); 56-65-5 (Adenosine Triphosphate); 64-69-7 (Iodoacetic Acid)

Record Date Created: 19940725

Record Date Completed: 19940725

4/9/16

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

08166825 94232701 PMID: 8177628

Assessing the need for anaerobic medium for the recovery of clinically significant blood culture **isolates in children.**

Dunne W M; Tillman J; Havens P L

Department of Pathology, Baylor College of Medicine, Houston, TX.

Pediatric infectious disease journal (UNITED STATES) Mar 1994, 13 (3) p203-6, ISSN 0891-3668 Journal Code: 8701858

Comment in Pediatr Infect Dis J. 1994 Sep;13(9) 837-8; Comment in PMID 7808863

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

We examined the sensitivity of several BACTEC media options for the detection of bacteremia and fungemia in children at two pediatric health care facilities. At one institution a single aerobic bottle containing PEDS Plus medium was as sensitive in identifying positive blood **cultures** as the combination of aerobic and anaerobic media (77% vs. 80%; P = 1.0). When data from both facilities were combined, a blood **culture** set containing both aerobic and anaerobic media detected significantly more positive blood **cultures** than any single aerobic medium. However, the aerobic/anaerobic bottle combination was not significantly better than a blood **culture** set containing two aerobic media and, in absolute terms, the latter identified more cases of bacteremia. Of the 116 clinically significant episodes of bacteremia identified in this study, only 1 was caused by an anaerobic bacterium. We conclude that the routine use of anaerobic media for blood **cultures** of pediatric patients might be unnecessary but that the use of two different aerobic media could increase the sensitivity of the BACTEC blood **culture** system.

Tags: Comparative Study; Human

Descriptors: Bacteremia--diagnosis--DI; *Bacteria --isolation and purification--IP; * **Culture** Media; *Fungemia--diagnosis--DI; Anaerobiosis; Candida--isolation and purification--IP; Child; **Enterobacter cloacae** --isolation and purification--IP; Porphyromonas--isolation and purification --IP; Retrospective Studies; Sensitivity and Specificity; Staphylococcus aureus--isolation and purification--IP

CAS Registry No.: 0 (Culture Media)
Record Date Created: 19940609
Record Date Completed: 19940609

4/9/17
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08159741 94225616 PMID: 8171679
Microbial studies of a tissue bank of cryopreserved human islet cells.
Lakey J R; Rajotte R V; Taylor G D; Kirkland T; Warnock G L
Surgical-Medical Research Institute, University of Alberta, Edmonton, Canada.
Transplantation proceedings (UNITED STATES) Apr 1994, 26 (2) p827, ISSN 0041-1345 Journal Code: 0243532
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Tags: Human; Support, Non-U.S. Gov't
Descriptors: Bacteria-- **growth** and development--GD; *Cryopreservation; *Islets of Langerhans; *Tissue Banks--standards--ST; Adult; Bacteria --isolation and purification--IP; **Enterobacter cloacae** -- **growth** and development--GD; **Enterobacter cloacae** --isolation and purification--IP; Prospective Studies; Pseudomonas-- **growth** and development--GD; Pseudomonas--isolation and purification--IP
Record Date Created: 19940602
Record Date Completed: 19940602

4/9/18
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08148931 94214801 PMID: 8162286
Bacteremia due to transplantation of contaminated cryopreserved pancreatic islets.
Taylor G D; Kirkland T; Lakey J; Rajotte R; Warnock G L
Department of Medicine, University of Alberta, Edmonton, Canada.
Cell transplantation (UNITED STATES) Jan-Feb 1994, 3 (1) p103-6, ISSN 0963-6897 Journal Code: 9208854
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
OBJECTIVE. To report two cases of pancreatic islet transplantation-related septicemia, and the results of an investigative protocol to identify potential sources of contamination. DESIGN. Case series. SETTING. University hospital clinical investigational islet transplantation program. RESULTS. The last two of our first seven islet transplantation recipients developed Enterobacter cloacae septicemia within hours of islet infusion. Both had received thawed cryopreserved islet infusions. No source of infection apart from islets could be identified. Pancreas harvesting and islet isolation protocols provided multiple opportunities for contamination. Environmental **cultures** during a mock islet isolation procedure failed to identify a source of Enterobacter. Previously cryopreserved islet lots were thawed and submitted for **culture**, 14/47 grew micro-organisms including E. cloacae in four instances. Following revision of protocols for aseptic handling of islets during processing and cryopreservation 55 consecutive pancreata undergoing processing were evaluated; 7 grew micro-organisms on arrival and in 3 cases these persisted through to cryopreservation. CONCLUSION. Two of seven islet transplantation recipients developed septicemia, likely related to infusion of contaminated cryopreserved islets. Using existing technology, for isolating islets from donor pancreata, recipients will remain at risk for this complication. Prevention should entail strict adherence to aseptic

technique, and, possibly, use of surveillance microbial **cultures** during the islet isolation process.
Tags: Case Report; Female; Human; Male
Descriptors: Bacteremia--etiology--ET; *Cryopreservation; *Diabetes Mellitus, Insulin-Dependent--surgery--SU; * **Enterobacter cloacae** --isolation and purification--IP; *Enterobacteriaceae Infections--etiology --ET; *Islets of Langerhans Transplantation--adverse effects--AE; Adult; Islets of Langerhans--cytology--CY; Tissue **Culture** --methods--MT
Record Date Created: 19940523
Record Date Completed: 19940523

4/9/19
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08073725 94139474 PMID: 8306813
Postantibiotic effect, and postantibiotic effect of subinhibitory concentrations, of sparfloxacin on gram-negative bacteria.
Odenholt-Tornqvist I; Bengtsson S
Department of Infectious Diseases, University Hospital, Uppsala, Sweden.
Chemotherapy (SWITZERLAND) Jan-Feb 1994, 40 (1) p30-6, ISSN 0009-3157 Journal Code: 0144731
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The postantibiotic effect (PAE), the postantibiotic sub-MIC effect (PA SME), and the sub-MIC effect (SME) of a new oral quinolone, sparfloxacin, were determined for different strains of gram-negative bacteria. A PAE was induced by 10 x MIC of sparfloxacin for 2 h and the antibiotic was then eliminated by washing and dilution. The PA SME was studied by adding different sub-MICs during the postantibiotic phase, and the SME by exposing the controls to the sub-MICs alone. **Growth** curves were followed for 20 h by continuous monitoring of optical density in an automatic incubator. Sparfloxacin induced a PAE of 0.9-2.4 h for all strains except two clinical strains of Enterobacter cloacae. In accordance with earlier experiments with sparfloxacin and gram-positive bacteria, this study showed a PA SME that was nearly equal to the PAE plus the effect of the subinhibitory concentration alone (SME).
Tags: Comparative Study
Descriptors: *Enterobacteriaceae--drug effects--DE; *Pseudomonas aeruginosa--drug effects--DE; *Quinolones--pharmacology--PD; Drug Resistance, Microbial; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Enterobacteriaceae-- **growth** and development--GD; Escherichia coli--drug effects--DE; Escherichia coli-- **growth** and development--GD; Klebsiella pneumoniae --drug effects--DE; Klebsiella pneumoniae-- **growth** and development--GD; Microbial Sensitivity Tests; Pseudomonas aeruginosa-- **growth** and development--GD
CAS Registry No.: 0 (Quinolones); 111542-93-9 (sparfloxacin)
Record Date Created: 19940317
Record Date Completed: 19940317

4/9/20
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08066203 94131950 PMID: 8300526
Electric fields induce curved growth **of Enterobacter cloacae, Escherichia coli, and Bacillus subtilis cells: implications for mechanisms of galvanotropism and bacterial** growth .
Rajnicek A M; McCaig C D; Gow N A
Department of Biomedical Sciences, Marischal College, University of Aberdeen, United Kingdom.
Journal of bacteriology (UNITED STATES) Feb 1994, 176 (3) p702-13, ISSN 0021-9193 Journal Code: 2985120R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Directional **growth** in response to electric fields (galvanotropism) is known for eukaryotic cells as diverse as fibroblasts, neurons, algae, and fungal hyphae. The mechanism is not understood, but all proposals invoke actin either directly or indirectly. We applied electric fields to bacteria (which are inherently free of actin) to determine whether actin was essential for galvanotropism. Field-treated (but not control) Enterobacter cloacae and Escherichia coli cells curved rapidly toward the anode. The response was both field strength and pH dependent. The direction of curvature was reversed upon reversal of field polarity. The directional **growth** was not due to passive bending of the cells or to field-induced gradients of tropic substances in the medium. Field-treated Bacillus subtilis cells also curved, but the threshold was much higher than for E. cloacae or E. coli. Since the curved morphology must reflect spatial differences in the rates of cell wall synthesis and degradation, we looked for regions of active wall **growth** . Experiments in which the cells were decorated with latex beads revealed that the anode-facing ends of cells grew faster than the cathode-facing ends of the same cells. Inhibitors of cell wall synthesis caused spheroplasts to form on the convex regions of field-treated cells, suggesting that the initial curvature resulted from enhanced **growth** of cathode-facing regions. Our results indicate that an electric field modulates wall **growth** spatially and that the mechanism may involve differential stimulation of wall **growth** in both anode- and cathode-facing regions. Electric fields may therefore serve as valuable tools for studies of bacterial wall **growth** . Use of specific E. coli mutants may allow dissection of the galvanotropic mechanism at the molecular level.

Tags: Support, Non-U.S. Gov't
Descriptors: Bacillus subtilis-- **growth** and development--GD; * **Enterobacter cloacae** -- **growth** and development--GD; *Escherichia coli-- **growth** and development--GD; Electricity; Hydrogen-Ion Concentration; Microscopy, Electron; Protein Synthesis Inhibitors--pharmacology--PD
CAS Registry No.: 0 (Protein Synthesis Inhibitors)
Record Date Created: 19940308
Record Date Completed: 19940308

4/9/21
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

08009814 94075533 PMID: 8253954
Cluster of Enterobacter cloacae pseudobacteremias associated with use of an agar slant blood culturing **system.**
Pearson M L; Pegues D A; Carson L A; O'Donnell R; Berger R H; Anderson R L; Jarvis W R
National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333.
Journal of clinical microbiology (UNITED STATES) Oct 1993, 31 (10) p2599-603, ISSN 0095-1137 Journal Code: 7505564
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

From 1 February through 12 October 1990, 27 blood **cultures** processed at Shiprock Hospital were positive for Enterobacter cloacae; only 3 had been reported in the preceding 12 months. Twenty (74%) of the **cultures** were obtained from patients without clinical evidence of gram-negative septicemia. The increase in E. cloacae-positive blood **cultures** was temporally associated with the introduction of a new blood **culturing** system. To evaluate potential risk factors for an E. cloacae-positive blood **culture** (case- **culture**), we conducted a case-control study. Case- **cultures** were compared with 81 randomly selected **cultures** that were processed during the epidemic period and that were not positive for E.

cloacae (controls). Because several factors suggested the possibility of pseudoinfection, we limited our analysis to the 20 blood **cultures** that appeared to be contaminants. Blood samples received in the laboratory during the midnight shift (5 of 20 [25%] versus 5 of 81 [6%]; odds ratio, 5.1; 95% confidence intervals, 1.01 to 24.6; P = 0.02) or present in the incubator with other E. cloacae-positive samples (17 of 20 [85%] versus 29 of 81 [36%]; odds ratio, 10.2, 95% confidence interval, 2.6 to 57.3; P < 0.001) were at increased risk for contamination. During mock experiments of the procedures for processing blood samples for **culture** , several breaks in aseptic technique and leakage from the blood **culturing** system were observed. **Cultures** of samples obtained from several environmental sites in the laboratory and the hand washings of two laboratory technicians grew E. cloacae.(ABSTRACT TRUNCATED AT 250 WORDS)

Tags: Human

Descriptors: Bacteremia--epidemiology--EP; *Bacteriological Techniques --standards--ST; * **Enterobacter cloacae** --isolation and purification--IP; *Enterobacteriaceae Infections--epidemiology--EP; Agar; Bacteremia --etiology--ET; Case-Control Studies; Cluster Analysis; Disease Outbreaks; Enterobacteriaceae Infections--etiology--ET; Quality Control

CAS Registry No.: 9002-18-0 (Agar)

Record Date Created: 19940110

Record Date Completed: 19940110

4/9/22

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

07992159 94057876 PMID: 8239327

Endophthalmitis caused by Enterobacter cloacae.

Milewski S A; Klevjer-Anderson P

Ophthalmology Department, University of Connecticut, Storrs.

Annals of ophthalmology (UNITED STATES) Aug 1993, 25 (8) p309-11, ISSN 0003-4886 Journal Code: 0210137

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Cataract extraction with placement of intraocular lenses is the most common intraocular procedure done today, with endophthalmitis as its most devastating complication. To our knowledge, this is only the third reported case of postoperative endophthalmitis caused by the gram-negative bacillus, Enterobacter cloacae. The course of infection, the treatment, and the laboratory identification of this organism are presented. It is important to add this proven case of gram-negative endophthalmitis to our **growing** knowledge of causes of this disease because, despite aggressive treatment with vitrectomy and intravitreal antibiotics, the infection was so virulent that it led to eventual phthisis bulbi.

Tags: Case Report; Female; Human

Descriptors: *Endophthalmitis--microbiology--MI; *Enterobacter cloacae; *Enterobacteriaceae Infections; *Eye Infections, Bacterial; Aged; Aged, 80 and over; Antibiotics, Combined--therapeutic use--TU; Cataract Extraction --adverse effects--AE; Endophthalmitis--therapy--TH; **Enterobacter cloacae** --isolation and purification--IP; Eye Enucleation; Lenses, Intraocular --adverse effects--AE; Vitrectomy; Vitreous Body--microbiology--MI

CAS Registry No.: 0 (Antibiotics, Combined)

Record Date Created: 19931201

Record Date Completed: 19931201

4/9/23

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

07903998 93364826 PMID: 8358668

A two-part energy burden imposed by growth **of Enterobacter cloacae and Escherichia coli in sodium dodecyl sulfate.**

Aspedon A; Nickerson K W

School of Biological Sciences, University of Nebraska, Lincoln 68588-0343.
Canadian journal of microbiology (CANADA) Jun 1993, 39 (6) p555-61, ISSN 0008-4166 Journal Code: 0372707
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Enterobacter cloacae, like most enteric bacteria, can **grow** in the presence of 10% sodium dodecyl sulfate (SDS). The bacteria tolerate the detergent and do not metabolize it. In a defined glucose-salts medium the **growth** rate remained unchanged (G = 55 min) as the detergent concentration was increased from 0 to 10% SDS. However, **growth** in SDS exhibited a two-part energy dependence. In part 1, the SDS- **grown** cells underwent rapid lysis when they ran out of energy. Cells that had entered stationary phase owing to carbon limitation lysed, while those that had entered owing to nitrogen or phosphorus limitation did not. We attribute part 1 of the energy dependence to SDS as a detergent. In part 2, the cells **grown** in 5 or 10% SDS exhibited longer lag periods, potassium accumulation, decreased cell yields, and higher oxygen consumption. The higher oxygen consumption occurred during both exponential phase and nitrogen-limited stationary phase. However, the decreased cell yield and higher oxygen consumption of SDS- **grown** cells were mimicked by cells **grown** in equivalent concentrations of sucrose or polyethylene glycol. We attribute part 2 of the energy dependence to SDS as a solute. Finally, with regard to the as yet unidentified bacterial osmotic stress detector, we used the micelle-forming nature of SDS to conclude that the detector was responding to turgor pressure-water activity rather than to osmolarity itself.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Energy Metabolism; *Enterobacter cloacae--metabolism--ME; *Escherichia coli--metabolism--ME; *Sodium Dodecyl Sulfate--pharmacology --PD; Bacteriolysis; Carbon--metabolism--ME; Cell Division; Drug Resistance, Microbial; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli --drug effects--DE; Escherichia coli-- **growth** and development--GD; Nitrogen--metabolism--ME; Osmotic Pressure; Oxygen Consumption; Phosphorus --metabolism--ME; Potassium--metabolism--ME

CAS Registry No.: 151-21-3 (Sodium Dodecyl Sulfate); 7440-09-7 (Potassium); 7440-44-0 (Carbon); 7723-14-0 (Phosphorus); 7727-37-9 (Nitrogen)

Record Date Created: 19930930
Record Date Completed: 19930930

4/9/24
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07842352 93297997 PMID: 8517752

Fate of Enterobacter cloacae JP120 and Alcaligenes eutrophus AEO106(pRO101) in soil during water stress: effects on culturability **and viability.**

Pedersen J C; Jacobsen C S

Department of Marine Ecology and Microbiology, National Environmental Research Institute, Roskilde, Denmark.

Applied and environmental microbiology (UNITED STATES) May 1993, 59 (5) p1560-4, ISSN 0099-2240 Journal Code: 7605801
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

A sandy loam soil near field capacity moisture content (psi = -0.050 MPa) or air dried (psi = -300 MPa) was inoculated with about 3 x 10(7) CFU of Enterobacter cloacae JP120 and Alcaligenes eutrophus AEO106(pRO101) per g and incubated in 40-g portions at 17 degrees C in closed or open Erlenmeyer flasks. In the field-moist soil, selective plating, direct viable counts,

and DNA hybridization showed only minor changes in the numbers of E. cloacae and A. eutrophus cells with time (14 days), and the results obtained with the three detection methods generally agreed. In the air-dried soil, the majority of both bacteria were found as intact DNA-carrying cells that were neither **culturable** nor viable by the methods employed in this study. The numbers of **culturable** E. cloacae and A. eutrophus cells dropped to 10(5) and 10(2) CFU/g, respectively, 2 h after inoculation. Direct viable counts showed that only about 1% of the cells detected by immunofluorescence microscopy were viable, but a fraction of viable nonculturable cells of both bacteria was present. A. eutrophus did not tolerate desiccation as well as E. cloacae. Only a minor fraction of the two test organisms regained their **culturability** or viability after rewetting of the air-dried soil; the number of total heterotrophic **culturable** bacteria, however, increased more than 10-fold and reached 73% of the level found in the field-moist soil at day 14.

Tags: Comparative Study; Support, Non-U.S. Gov't

Descriptors: Alcaligenes--isolation and purification--IP; * **Enterobacter cloacae** --isolation and purification--IP; *Soil Microbiology; Alcaligenes --genetics--GE; Alcaligenes-- **growth** and development--GD; Bacteriological Techniques; Base Sequence; Colony Count, Microbial; DNA, Bacterial --genetics--GE; Enterobacter cloacae--genetics--GE; **Enterobacter cloacae** -- **growth** and development--GD; Evaluation Studies; Microscopy, Fluorescence; Molecular Sequence Data; Nucleic Acid Hybridization; Reproducibility of Results; Water

CAS Registry No.: 0 (DNA, Bacterial); 7732-18-5 (Water)

Record Date Created: 19930721

Record Date Completed: 19930721

4/9/25

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

07782972 93238469 PMID: 8477572

Effect of antibiotics on endotoxin release from gram-negative bacteria.

Eng R H; Smith S M; Fan-Havard P; Ogbara T

Infectious Disease Section, Department of Veterans Affairs Medical Center, East Orange, NJ 07018-1095.

Diagnostic microbiology and infectious disease (UNITED STATES) Mar-Apr 1993, 16 (3) p185-9, ISSN 0732-8893 Journal Code: 8305899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Antibiotics may inhibit bacterial **growth** or may kill bacteria by inhibiting cell wall synthesis or protein synthesis. The amount of endotoxin released during antibiotic action has been found to be clinically important. Nine antibiotics, representing seven classes, were studied for the amounts of endotoxin released during their action on susceptible strains of Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, and Pseudomonas aeruginosa. Staphylococcus aureus, which produces no endotoxin, was used as a control organism. Aztreonam induced the highest release of endotoxin, whereas other antibiotics such as imipenem and the quinolones induced the lowest release of endotoxin. Although the quantities of endotoxin released are not easily explained from the established mechanisms of antibiotic action, our findings may have implications for therapy of the acutely ill, septic patient in whom release of large quantities of endotoxin may be catastrophic.

Tags: Human

Descriptors: *Antibiotics--pharmacology--PD; *Endotoxins--metabolism--ME; *Gram-Negative Bacteria--drug effects--DE; Antibiotics--classification--CL; Enterobacter cloacae--drug effects--DE; **Enterobacter cloacae** -- **growth** and development--GD; Escherichia coli--drug effects--DE; Escherichia coli -- **growth** and development--GD; Gram-Negative Bacteria-- **growth** and development--GD; Klebsiella pneumoniae--drug effects--DE; Klebsiella pneumoniae-- **growth** and development--GD; Pseudomonas aeruginosa--drug effects--DE; Pseudomonas aeruginosa-- **growth** and development--GD

CAS Registry No.: 0 (Antibiotics); 0 (Endotoxins)

Record Date Created: 19930526
Record Date Completed: 19930526

4/9/26
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07610951 93066028 PMID: 1438073
Microorganisms associated with natural fermentation of Prosopis africana seeds for the production of okpiye.
Achi O K
Department of Science Technology, Federal Polytechnic, Idah, Nigeria.
Plant foods for human nutrition (Dordrecht, Netherlands) (NETHERLANDS) Oct 1992, 42 (4) p297-304, ISSN 0921-9668 Journal Code: 8803554
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Okpiye is a food condiment prepared by the fermentation of Prosopis africana seeds. The traditional process for the production and microbiological characteristics of the condiment were investigated. During laboratory fermentation that lasted 96 h, the mesquite seeds underwent a natural fermentation that was characterised by the **growth** of microorganisms to 10(6)-10(8) cfu/g. Several species of bacteria especially B. subtilis, B. licheniformis, B. megaterium, Staphylococcus epidermidis and Micrococcus spp were found to be the most actively involved organisms. However, significant contributions to the microbial ecology were made by Enterobacter cloacae and Klebsiella pneumoniae. Lactobacillus spp were present in low numbers towards the end of the fermentation. The presence of Proteus and Pseudomonas spp in traditional fermented samples demonstrate the variability which may exist in the microflora of individual fermented samples. Variations in the important microbial groups show that Bacillus spp were the most prevalent species and occurred until the end of fermentation. Temperature, pH and titratable acidity varied with time and were influenced by the metabolic activities of the microorganisms.
Descriptors: *Condiments--microbiology--MI; *Fabaceae--microbiology--MI; *Fermentation; *Food Microbiology; *Plants, Medicinal; *Seeds--microbiology --MI; Bacillus-- **growth** and development--GD; Bacillus--isolation and purification--IP; Colony Count, Microbial; **Enterobacter cloacae** -- **growth** and development--GD; **Enterobacter cloacae** --isolation and purification --IP; Klebsiella pneumoniae-- **growth** and development--GD; Klebsiella pneumoniae--isolation and purification--IP; Lactobacillus-- **growth** and development--GD; Lactobacillus--isolation and purification--IP; Micrococcus-- **growth** and development--GD; Micrococcus --isolation and purification--IP; Proteus-- **growth** and development--GD; Proteus --isolation and purification--IP; Pseudomonas-- **growth** and development--GD ; Pseudomonas--isolation and purification--IP; Staphylococcus epidermidis -- **growth** and development--GD; Staphylococcus epidermidis--isolation and purification--IP
Record Date Created: 19921202
Record Date Completed: 19921202

4/9/27
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07487490 92351057 PMID: 1641601
Enterobacter endocarditis.
Tunkel A R; Fisch M J; Schlein A; Scheld W M
Division of Infectious Diseases, Medical College of Pennsylvania, Philadelphia 19129.
Scandinavian journal of infectious diseases (SWEDEN) 1992, 24 (2) p233-40, ISSN 0036-5548 Journal Code: 0215333
Contract/Grant No.: RO1-AI17904; AI; NIAID; T32-AI07046; AI; NIAID
Document type: Journal Article; Review; Review of Reported Cases
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Endocarditis due to Enterobacter species is very rare. We recently cared for a patient who developed E. cloacae endocarditis following mitral valve replacement with a porcine heterograft, and was successfully treated with antibiotic therapy alone. A review of the literature disclosed an additional 17 well-described cases of enterobacter endocarditis. Two-thirds of the patients had underlying cardiac disease. The mitral valve was most frequently involved (10/16 cases) with 4 of the patients having concomitant aortic valve involvement. The overall mortality rate was 44.4%. Antibiotic therapy of enterobacter endocarditis should consist of the combination of a beta-lactam antibiotic and an aminoglycoside with careful monitoring of blood **cultures** to assure the adequacy of therapy. Resistance of enterobacter to previously susceptible antibiotics may occur during therapy due to induction of a chromosomally-mediated beta-lactamase, necessitating a change in antimicrobial therapy. Valvular surgery is indicated for patients failing medical management. (45 Refs.)

Tags: Case Report; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: Endocarditis, Bacterial--microbiology--MI; * **Enterobacter cloacae** --isolation and purification--IP; *Enterobacteriaceae Infections --microbiology--MI; Middle Age

Record Date Created: 19920901
Record Date Completed: 19920901

4/9/28

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07472231 92335780 PMID: 1631483

Influence of transient salivary flora on assessment of mutans streptococci level by the "Strip mutans" method.

el-Nadeef M; Kalfas S; Edwardsson S; Ericson D

Department of Cariology, Faculty of Odontology, Lund University, Malmo, Sweden.

Scandinavian journal of dental research (DENMARK) Jun 1992, 100 (3) p149-53, ISSN 0029-845X Journal Code: 0270023

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: DENTAL; INDEX MEDICUS

The Dentocult SM ("Strip mutans") method occasionally shows decoloration of broth and of colonies of mutans streptococci on the plastic strip, thereby making interpretation difficult. In an attempt to explain the phenomenon and to investigate the influence of the salivary flora on the "Strip mutans" method, a total of 46 subjects were sampled. Saliva was analyzed using the "Strip mutans" method and conventional plating techniques to identify mutans streptococci, enterococci, staphylococci, enteric bacteria, and yeasts. Approximately 85% of the "Strip mutans" scores coincided with the conventional MSB-plating method. Two samples showed decolored mutans streptococci colonies on the "Strip mutans" strip. Enterococcus spp. were present in the saliva of these test subjects and could **grow** in the "Strip mutans" broth. Enterococcus faecalis was able to induce the same type of decoloration under experimental pure **culture** conditions. Three "Strip mutans" samples showed small colonies of mutans streptococci, visible only under magnification (x 10-20). Staphylococcus epidermidis was present in these saliva samples and showed heavy **growth** in the broth. Under experimental pure **culture** conditions S. epidermidis also inhibited the **growth** of mutans streptococci to some extent.

Tags: Human

Descriptors: *Bacteria--isolation and purification--IP; *Reagent Strips --diagnostic use--DU; *Saliva--microbiology--MI; *Streptococcus mutans --isolation and purification--IP; Adult; Bacteria-- **growth** and development --GD; Colony Count, Microbial; **Enterobacter cloacae** -- **growth** and development--GD; **Enterobacter cloacae** --isolation and purification--IP; Enterobacteriaceae-- **growth** and development--GD; Enterobacteriaceae

--isolation and purification--IP; Enterococcus-- **growth** and development --GD; Enterococcus--isolation and purification--IP; Enterococcus faecalis -- **growth** and development--GD; Enterococcus faecalis --isolation and purification--IP; Escherichia coli-- **growth** and development--GD; Escherichia coli--isolation and purification--IP; Middle Age; Staphylococcus aureus-- **growth** and development--GD; Staphylococcus aureus --isolation and purification--IP; Staphylococcus epidermidis-- **growth** and development--GD; Staphylococcus epidermidis--isolation and purification --IP; Streptococcus mutans-- **growth** and development--GD; Yeasts-- **growth** and development--GD; Yeasts--isolation and purification--IP
CAS Registry No.: 0 (Reagent Strips)
Record Date Created: 19920820
Record Date Completed: 19920820

4/9/29
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07450719 92314252 PMID: 1352150
Molecular analysis provides evidence for the endogenous origin of bacteremia and meningitis due to Enterobacter cloacae in an infant.
Lambert-Zechovsky N; Bingen E; Denamur E; Brahimi N; Brun P; Mathieu H; Elion J
Laboratoire de Microbiologie, Hopital Robert Debre, Paris, France.
Clinical infectious diseases - an official publication of the Infectious Diseases Society of America (UNITED STATES) Jul 1992, 15 (1) p30-2, ISSN 1058-4838 Journal Code: 9203213
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
We analyzed the restriction fragment length polymorphism (RFLP) of total DNA and of ribosomal DNA regions (ribotyping) to document the occurrence of endogenous, systemic bacteremia and meningitis due to Enterobacter cloacae in a newborn. Five strains of E. cloacae were isolated from this newborn. Three of these strains were recovered from stool at counts of 10(8), 10(9), and 10(9) organisms/g of feces, respectively; one strain was isolated from blood; and one strain was isolated from cerebrospinal fluid. In addition, five epidemiologically unrelated strains of E. cloacae were studied for comparison. Our study clearly shows the genetic relatedness of the strains isolated sequentially from **cultures** of stool, blood, and cerebrospinal fluid. RFLP analysis of total DNA and ribotyping seem particularly well suited to the study of the epidemiology of nosocomial E. cloacae strains.
Tags: Case Report; Human; Male
Descriptors: *Bacteremia--microbiology--MI; *DNA, Bacterial--analysis--AN ; *Enterobacter cloacae--genetics--GE; *Enterobacteriaceae Infections --etiology--ET; *Meningitis, Bacterial--microbiology--MI; DNA, Ribosomal --analysis--AN; **Enterobacter cloacae** --isolation and purification--IP; Enterobacteriaceae Infections--diagnosis--DI; Infant, Newborn; Polymorphism, Restriction Fragment Length
CAS Registry No.: 0 (DNA, Bacterial); 0 (DNA, Ribosomal)
Record Date Created: 19920806
Record Date Completed: 19920806

4/9/30
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07436471 92299993 PMID: 1351497
Handwashing and disinfection of heavily contaminated hands--effective or ineffective?
Kjolen H; Andersen B M
Department of Pharmacy, University Hospital, Tromso, Norway.
Journal of hospital infection (ENGLAND) May 1992, 21 (1) p61-71, ISSN 0195-6701 Journal Code: 8007166
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Hands are among the principal vehicles for transfer of nosocomial pathogens in hospitals. Often, outbreaks of infection are thought to be caused by a lack of compliance with handwashing guidelines, rather than due to the inadequacy of the handwashing agents used. In this study the effectiveness of proper handwashing and the use of three different hand disinfectants: ethanol 70% (E), isopropanol 40% (I) and alcoholic chlorhexidine (70%) (AC) was compared using three volunteers whose fingertips were heavily contaminated with a succession of bacteria including: Enterococcus faecalis, Staphylococcus aureus, Escherichia coli and Enterobacter cloacae. After each contamination, thorough handwashing and application of one disinfectant on the hands were performed three times. Fingerprint-samples were taken before and 1 min after application of the disinfectants. Thorough handwashing with an ordinary liquid soap ('Sterisol') did not reduce the confluent **growth** of bacteria on fingertips for any of the species used (197 examinations). Only AC had a significant effect on fingers heavily contaminated with S. aureus (126 examinations; AC compared with E and I; P less than 0.0002 and P less than 0.0002 respectively), but did not completely eradicate the bacteria. After contamination with Ent. cloacae (118 examinations), none of the three agents were particularly effective, but E and AC seemed to be somewhat more effective than I (P less than 0.0002 and P less than 0.01 respectively). When successive contamination was performed using all bacterial species, AC was the most effective decontaminant. However, Ent. cloacae was still present on the fingertips after 15 repeated courses of handwashing and applications of disinfectants. Bathing of hands in AC for 20s completely eradicated all bacteria from the hands. The study demonstrates that, when heavily contaminated, an ordinary handwashing followed by disinfectants is not enough to eradicate potentially pathogenic bacteria from the hands.

Tags: Comparative Study; Female; Human; Male

Descriptors: *1-Propanol--therapeutic use--TU; *Chlorhexidine --therapeutic use--TU; *Cross Infection--prevention and control--PC; *Enterobacter cloacae--drug effects--DE; *Enterococcus faecalis --drug effects--DE; *Escherichia coli--drug effects--DE; *Ethanol--therapeutic use --TU; *Handwashing--methods--MT; *Staphylococcus aureus--drug effects--DE; **Enterobacter cloacae** --isolation and purification--IP; Enterococcus faecalis--isolation and purification--IP; Escherichia coli--isolation and purification--IP; Hospitals; Staphylococcus aureus --isolation and purification--IP

CAS Registry No.: 55-56-1 (Chlorhexidine); 64-17-5 (Ethanol); 71-23-8 (1-Propanol)

Record Date Created: 19920723
Record Date Completed: 19920723

4/9/31

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07363357 92226524 PMID: 1373422

Application and assessment of cloacin typing of Enterobacter cloacae.

Daw M A; Corcoran G D; Falkiner F R; Keane C T
Department of Clinical Microbiology, Trinity College, Dublin, Ireland.

Journal of hospital infection (ENGLAND) Mar 1992, 20 (3) p141-51, ISSN 0195-6701 Journal Code: 8007166

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Three methods, O-serotyping, phage typing and susceptibility to bacteriocins, were used to type 357 clinical isolates of Enterobacter cloacae **cultured** from 219 patients. One hundred and sixty isolates were typed by serology and phage typing. When these two methods were used, primary classification of isolates was based on serology (65.7% typable) and phage typing for further subdivision (94.1% typable). When all the

isolates were typed by cloacin susceptibility, 81.5% of them were typable. Maximum discrimination between **cultures** was achieved when the three methods were used together; no single method was sufficiently discriminatory. There was a close parallel between serotyping and bacteriocin lysis pattern. The latter was easy to perform and the results were achieved within 48 h. By applying this typing system two episodes of cross-infection were identified in a haematology/oncology unit and intensive care unit.

Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Descriptors: *Bacteriophage Typing; *Cloacin--isolation and purification --IP; *Enterobacter cloacae--classification--CL; *Serotyping--methods--MT; **Enterobacter cloacae** -- **growth** and development--GD; Feces--microbiology --MI; Nose--microbiology--MI; O Antigens; Pharynx--microbiology--MI; Polysaccharides, Bacterial--isolation and purification--IP; Seroepidemiolog ic Studies

CAS Registry No.: 0 (O Antigens); 0 (Polysaccharides, Bacterial); 37370-19-7 (Cloacin)

Record Date Created: 19920521

Record Date Completed: 19920521

4/9/32

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2004 The Dialog Corp. All rts. reserv.

07339253 92202367 PMID: 1551974

Bacteriophage lytic patterns for identification of salmonellae, shigellae, Escherichia coli, Citrobacter freundii, and Enterobacter cloacae.

He X Q; Pan R N

Center for Medical Cultures Collection (Bacteria), Jiangxi Hygienic and Antiepidemic Station, Nanchang, People's Republic of China.

Journal of clinical microbiology (UNITED STATES) Mar 1992, 30 (3) p590-4, ISSN 0095-1137 Journal Code: 7505564

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A series of bacteriophages specific for Escherichia coli (E-1, E-2, E-3, and E-4), Citrobacter freundii (phi I, phi II, and phi III), Enterobacter cloacae (Ent), and Shigella spp. (Sh) have been isolated from hospital sewage. These bacteriophages, in combination with Felix Salmonella phage O-I, were used as a diagnostic phage typing set which included seven phage preparations: O-I, C (phi I and phi III), Sh, E (E-1 and E-2), CE (phi II and E-3), E-4, and Ent. After 20,280 **cultures** of 27 species and 9 biogroups of 15 genera of the family Enterobacteriaceae and 276 **cultures** of 8 species of 6 genera outside the Enterobacteriaceae were tested, it was shown that most strains of salmonellae, E. coli, C. freundii, and E. cloacae can be identified accurately. The sensitivities of identification were 83.6% for E. cloacae, 88.8% for C. freundii, 90.3% for E. coli, and 95.76% for salmonellae. The specificities were 99.78% for salmonellae, 99.84% for E. cloacae, 99.89% for E. coli, and 99.97% for C. freundii. The results of bacteriophage lytic patterns were highly correlated with Shigella serotypes. Therefore, such a phage typing set may be used routinely in public hygiene and clinical laboratories.

Tags: Human

Descriptors: *Bacteriophage Typing; *Enterobacteriaceae--classification --CL; Citrobacter freundii--classification--CL; Citrobacter freundii --isolation and purification--IP; Enterobacter cloacae--classification--CL; **Enterobacter cloacae** --isolation and purification--IP; Enterobacteriaceae --isolation and purification--IP; Escherichia coli--classification--CL; Escherichia coli--isolation and purification--IP; Evaluation Studies; Salmonella--classification--CL; Salmonella--isolation and purification--IP ; Serotyping; Shigella--classification--CL; Shigella --isolation and purification--IP

Record Date Created: 19920429

Record Date Completed: 19920429

4/9/33
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2004 The Dialog Corp. All rts. reserv.

07254908 92117551 PMID: 1768093

Growth **kinetics of coliform bacteria under conditions relevant to drinking water distribution systems.**

Camper A K; McFeters G A; Characklis W G; Jones W L

Center for Interfacial Microbial Process Engineering, Montana State University, Bozeman 59717.

Applied and environmental microbiology (UNITED STATES) Aug 1991, 57 (8) p2233-9, ISSN 0099-2240 Journal Code: 7605801

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The **growth** of environmental and clinical coliform bacteria under conditions typical of drinking water distribution systems was examined. Four coliforms (Klebsiella pneumoniae, Escherichia coli, Enterobacter aerogenes, and Enterobacter cloacae) were isolated from an operating drinking water system for study; an enterotoxigenic E. coli strain and clinical isolates of K. pneumoniae and E. coli were also used. All but one of the coliforms tested were capable of **growth** in unsupplemented mineral salts medium; the environmental isolates had greater specific **growth** rates than did the clinical isolates. This trend was maintained when the organisms were **grown** with low levels (less than 1 mg liter-1) of yeast extract. The environmental K. pneumoniae isolate had a greater yield, higher specific **growth** rates, and a lower Ks value than the other organisms. The environmental E. coli and the enterotoxigenic E. coli strains had comparable yield, **growth** rate, and Ks values to those of the environmental K. pneumoniae strain, and all three showed significantly more successful **growth** than the clinical isolates. The environmental coliforms also grew well at low temperatures on low concentrations of yeast extract. Unsupplemented distribution water from the collaborating utility supported the **growth** of the environmental isolates. **Growth** of the K. pneumoniae water isolate was stimulated by the addition of autoclaved biofilm but not by tubercle material. These findings indicate that **growth** of environmental coliforms is possible under the conditions found in operating municipal drinking water systems and that these bacteria could be used in tests to determine assimilable organic carbon in potable water.

Tags: Support, Non-U.S. Gov't

Descriptors: Enterobacteriaceae-- **growth** and development--GD; *Water Microbiology; *Water Supply; Enterobacter-- **growth** and development--GD; Enterobacter--isolation and purification--IP; **Enterobacter cloacae** -- **growth** and development--GD; **Enterobacter cloacae** --isolation and purification--IP; Enterobacteriaceae--isolation and purification--IP; Escherichia coli-- **growth** and development--GD; Escherichia coli --isolation and purification--IP; Kinetics; Klebsiella pneumoniae-- **growth** and development--GD; Klebsiella pneumoniae--isolation and purification --IP; Temperature

Record Date Created: 19920220

Record Date Completed: 19920220

?logoff hold

12jan04 12:00:02 User228206 Session D2103.20

$5.81 1.817 DialUnits File155

$6.93 33 Type(s) in Format 9

$6.93 33 Types

$12.74 Estimated cost File155

$0.46 TELNET

$13.20 Estimated cost this search

$13.74 Estimated total session cost 1.905 DialUnits

Status: Signed Off. (2 minutes)